A Dissertation on

STUDY ON THE EFFECT OF GLYCEMIC CONTROL ON MEAN PLATELET VOLUME IN TYPE 2 DIABETIC PATIENTS ON TREATMENT

Submitted to

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY
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In partial fulfilment of the Regulations
for the Award of the Degree of

M.D. BRANCH - I

GENERAL MEDICINE

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CERTIFICATE BY THE INSTITUTION

This is to certify that **Dr. DORON SUSAN MATHEW,** Post - Graduate Student (May 2012 TO April 2015) in the Department of General Medicine STANLEY MEDICAL COLLEGE, Chennai- 600 001, has done this dissertation on "**STUDY ON THE EFFECT OF GLYCEMIC CONTROL ON MEAN PLATELET VOLUME IN TYPE 2 DIABETIC PATIENTS ON TREATMENT"** under my guidance and supervision in partial fulfillment of the regulations laid down by the Tamilnadu Dr. M. G. R. Medical University, Chennai, for M.D. (General Medicine), Degree Examination to be held in April 2015.

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DECLARATION

I, **Dr. DORON SUSAN MATHEW,** declare that I carried out this work on "**STUDY ON THE EFFECT OF GLYCEMIC CONTROL ON MEAN PLATELET VOLUME IN TYPE 2 DIABETIC PATIENTS ON TREATMENT**" at the Diabetology OPD and Medical wards of Government Stanley Hospital during the period March 2014 to September 2014. I also declare that this bonafide work or a part of this work was not submitted by me or any other for any award, degree, or diploma to any other university, board either in India or abroad.

This is submitted to The Tamilnadu DR. M. G. R. Medical University, Chennai in partial fulfilment of the rules and regulation for the M. D. Degree examination in General Medicine.

Dr.DORON SUSAN MATHEW

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ABBREVIATIONS

T3	:	T3-Triiodothyronine
T4	:	T4-Thyroxine
TSH	:	Thyroid Stimulating Hormone
HbA1c	:	Glycosylated Haemoglobin
FPG	:	Fasting Plasma Glucose
PPBG	:	Post Prandial Blood Glucose
MPHA	:	Megakaryote- platelet hemostatic axis
LDL	:	Low Density Lipoproteins
TGL	:	Triglycerides
HDL	:	High density lipoproteins
MPV	:	Mean platelet volume
IDF	:	International diabetes federation
ADA	:	American Diabetes Assocation
OHA	:	Oral hypoglycemic agents
SEAR	:	South East Asian Region
GDM	:	Gestational Diabetes Mellitus
ICMR	:	Indian Council of Medical Research
LADA	:	Latent Autoimmune Diabetes in adults
GAD	:	Glutamic acid decarboxylase
MODY	:	Maturity onset diabetes of young
DCCT	:	Diabetes control and complication trial

NGSP	:	Nationalised glycolhemoglobin standardisation programme
OGTT	:	Oral glucose tolerance test
UKPDS	:	United Kingdom prospective diabetes study
ADP	:	Adenosine Diphosphate
BMI	:	Body mass index
2,3 DPG	:	2,3 Diphosphoglycerate
RBC	:	Red blood cell
vWF	:	von Willebrand Factor
PDW	:	Platelet distribution width
PCT	:	Plateletcrit
PLCR	:	Platelet large cell ratio
LDH	:	Lactate dehydrogenase
Tx A2	:	Thromboxane A2
NO	:	Nitric oxide
PDEGF	:	Platelet derived epidermal growth factor
IGF 1	:	Insulin like growth factor 1
PF4	:	Platelet factor 4
PAI	:	Plasminogen activator inhibitor

CONTENTS

INSTITUTIONAL ETHICAL COMMITTEE, STANLEY MEDICAL COLLEGE, CHENNAI-1

Title of the Work : Study on the effect of Glycemic control on mean Platelet volume in type 2 diabetic patients on treatment.

Principal Investigator : Dr. Doron Susan Mathew

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The request for an approval from the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 02.07.2014 at the Council Hall, Stanley Medical College, Chennai-1 at 2PM

The members of the Committee, the secretary and the Chairman are pleased to approve the proposed work mentioned above, submitted by the principal investigator.

The Principal investigator and their team are directed to adhere to the guidelines given below:

1. You should inform the IEC in case of changes in study procedure, site investigator investigation or guide or any other changes.
2. You should not deviate from the area of the work for which you applied for ethical clearance.
3. You should inform the IEC immediately, in case of any adverse events or serious adverse reaction.
4. You should abide to the rules and regulation of the institution(s).
5. You should complete the work within the specified period and if any extension of time is required, you should apply for permission again and do the work.
6. You should submit the summary of the work to the ethical committee on completion of the work.

K Vasanthan

MEMBER SECRETARY,
IEC, SMC, CHENNAI

ABSTRACT

Introduction

Diabetes mellitus is a global pandemic. The increased platelet activity may play a role in the development of vascular complications of this metabolic disorder. The mean platelet volume (MPV) is an indicator of the average size and activity of platelets. Larger platelets are younger and exhibit more activity.

Increased mean platelet volume is a known risk factor for various acute vascular complications, which is commonly associated with patients with diabetes mellitus. This study was aimed to investigate the association of Mean Platelet Volume (MPV) with glycemic control in Type 2 Diabetes Mellitus (DM).

Material and Methods

A total of 100 patients were selected and allocated to three Groups according to their HbA1C level. Investigations like fasting blood glucose, HbA1Cand MPV were performed. Relation of MPV was assessed with HbA1C and FBS, PPBS, duration of diabetes. To find the significance difference between the bivariate samples in independent groups the Independent sample t-test was used. For the multivariate analysis the one way ANOVA was used. In both the above statistical tools the probability value .05 is considered as significant level.

Results

The mean platelet counts and MPV were higher in diabetics with poor glycemic control defined as HbA1C more eight {[7.29+/-.786(<7)], [7.9+/-.659(7.1-8)] and [8.76+/-1.068(>8)fl] than compared to the patients with good control. MPV showed a strong positive correlation with HbA1C levels (P=0.001).

Conclusion

This study has shown an elevation in Mean Platelet Volume in patients with increased HbA1C (glycated hemoglobin) values, thus indicating poor control of diabetes and, it can be stated that an increase in Mean Platelet Volume is directly proportional to the numerical value of HbA1C (glycated hemoglobin) and inversely related to the control of diabetes. Statistically significant association was found with glycated hemoglobin (HbA1C) (P-value =.0001) and mean platelet volume.

Keywords: Diabetes mellitus, glycemic control,HbA1C(glycated hemoglobin), mean platelet volume

INTRODUCTION

Diabetes mellitus is a rapidly increasing endocrinological disorder in both developed as well as developing nations.

Diabetes mellitus is a disease of antiquity known to mankind since past 3500 years. Ancient Indian scholars like Charak and Sushrutha recorded about this in the past. It is a big concern because of the devastating effects of its complications.

Mean Platelet Volume (MPV) is a new and independent risk factor for atherosclerosis. Studies have shown that increased MPV is a risk factor for transient ischemic attack, myocardial infarction, and cerebral ischemia[1]. Altered platelet morphology and function have been reported in patients with Diabetes Mellitus (DM) and MPV was found to be significantly higher in diabetic patients[2,3], thereby playing role in the micro- and macro-vascular complications of diabetic patients. The prevalence of diabetic microvascular complications is more in people with poor glycemic control and longer duration of DM[4].

A large proportion of patients with Type 2 DM suffer from preventable vascular complications. There is a need to develop risk

factor modification interventions to reduce the impact of long term complications. Study by Kodiatte TA et al., showed that in diabetes mellitus, platelets become more reactive and their Mean

Volume (MPV) is increased. The increased platelet size may be one factor in the increased risk of atherosclerosis associated with diabetes mellitus and associated vascular complications. Hence, MPV would be a useful prognostic marker of cardio-vascular complications in diabetes.

Although the underlying mechanism of higher MPV in diabetic subjects is incompletely understood, but thought to be due to osmotic swelling as a result of hyperglycemia [5]. Alternatively,increased platelet size may reflect the presence of high platelet turnover and younger platelets[6].

Study by Shah B et al., showed that mean platelet volume is strongly and independently associated with the presence and severity of diabetes. The association between MPV and diabetes was most apparent in those with the poorest glucose control[7].

AIM OF THE STUDY

To study the effect of glycemic control on mean platelet volume among Type II diabetic patients on treatment.

REVIEW OF LITERATURE

DIABETES

Diabetes mellitus refers to a group of common metabolic disorders consisting of different subtypes of diabetes with hyperglycemia due to insulin deficiency, either absolute or relative as a common factor. Diabetes mellitus exist in several distinct forms and is caused by several complex interaction of environmental and genetic factors. The prevalence of diabetes mellitus has risen dramatically over the past few decades from an estimated thirty million cases in 1985 to 177 million in 2000 to 382 million in 2013 according to the International diabetes federation 2013,diabetes atlas 6th edition.[8] Based on current trends,>592 million individuals will have Diabetes by the year 2032.

Diseases with cardinal features of diabetes mellitus were recognized in ancient times. Georg Ebers discovered an Egyptian papyrus from 1550 BC which described a polyuric state. The term diabetes was first used by Aretaeus from Cappadocia, from the word syphon which in Greek means the fluid does not remain in the body, but the man's body is used as a channel. The Hindu physicians, Charak

and Sushrut,where probably the first to recognize the sweetness of diabetic urine which was recorded between 400 and 500 BC.

The first description of hyperglycemia was published in 1776 in a paper by Matthew Dobson of Liverpool[9]. In 1815 the sugar in diabetic urine was proved to be glucose or grape sugar by the French chemist Michel Chevreul[10]. Between 1846 and 1848 a French physiologist, Claude Bernard hypothesized the glycogenic theory thus clarifying the glucose metabolism [11] in 1869 Paul Langerhans discovered and described an island of cells from pancreatic tissue and in 1893 ,Gustave Laguesse suggested internal secretions from the island of cells isolated from the pancreas and named them islets of Langerhans [12],[13]. In 1909 the glucose lowering internal secretion of the islets was named by the Belgian jean de Meyer as insulin[Latin island]. The term insulin was given by Macleod unaware of de Meyer's earlier suggestion of insuline[14]

Banting and best where the first to discover insulin as a therapeutic agent, in 1922 the first clinical trial of insulin was done with an extract made by Best. Frederick Sanger reported the amino acid sequence of insulin in 1955[15]. Dorothy Hodgkin in 1969 the three dimensional structure of insulin[16]. Wang Ying-lai and his colleagues

In Shanghai synthesized complete insulin molecule from amino acids in 1965[17].

EPIDEMIOLOGY

The prevalence of diabetes has increased by leaps and bounds in India and has reached epidemic proportions. India has more than 62 million diabetic patients. Thus it is vital to epidemiological data on diabetes from all over the world. According to international diabetes federation 2013 in china has the largest population of diabetics of about 98.4 million, India being second with 65.1 million and USA 24.4 million diabetics. IDF 2013 also gives the data of total diabetics in the world to be around 382 million which is estimated to rise by around 55% to reach 592 million diabetic population by the year 2032. The study also gives the data of SEAR countries to inhabit 72.1 million of diabetic population in 2013 which is postulated to increase to 123 million by 2032 that is a 71% rise from the present diabetic population.[18]

Definitive data from population based studies on prevalence of type 1 diabetes is not available from India. However, it is relatively rare in our country and less than 2% of the diabetics in India are having type 1 diabetes. Asian continent has lowest incidence rate of type1

diabetes, approximately 0.5cases per annum per lakh population. However recently it has been postulated that some patients who have onset of diabetes in the middle age and whose symptoms develop gradually and who develop either primary failure or early secondary failure to sulfonylureas, are actually suffering from late onset and slowly progressing subtype of type 1 diabetes. Immunological markers for type 1 diabetes are positive in these patients. There are few studies on these patients from south India, but epidemiological studies are lacking.

Prevalence of type 1 diabetes increases as one travels from southern to northern hemisphere. About 15-20% of diabetics in northern European countries are having type 1 diabetes. Among the countries in the European continent, there are significant north south difference as regards incidence. Incidence rate of type 1 diabetes in Finland28 per 1 lakh as against 6 per 1 lakh in France. In addition to geographical variation there is a seasonal variation in the incidence rate. More cases are diagnosed in winter. This is attributed to seasonal variation for viral infection which trigger autoimmune destruction of beta cells in pancreas leading toacute onset diabetes. An interesting finding about incidence is that in USA, incidence is much higherin white population as compared to blacks in the same area. Since the

environmental factors are same for both the ethnic groups, the difference in incidence isprobably based on genetic factors. Offspring oftype 1 diabetic father are 3 times more likely to develop it by the age of 20 years as compared to that of type 1 diabetic mother (6%vs2%). It is postulated that exposure to diabetic environment in utero offers protection, perhaps by inducing immunological tolerance to the antigen involved in autoimmune destruction of pancreatic beta cells. However genetic factors are less important in pathogenesis of type 1 diabetes as compared to type 2 diabetes. This has been amply true by the studies done in twins.

Relationship between type1 diabetes occurrence and certain HLA antigens: in the early seventies, certain HLA antigens were shown to be positively associated with type 1 diabetes but not with type 2 diabetes. Although initially certain HLA B antigens were identified for association with type 1 diabetes, DR antigens have since been shown to have stronger association with the disease. In all the population studied, type 1 diabetes has been confined largely to the individuals who carry HLA DR 3 or HLADR4 antigen.

As against incidence studies in type 1 diabetes, prevalence studies are more commonly done in type 2diabetes. It has become

epidemic in many developing and rapidly industrializing countries including India. In our country more than 96% of diabetics have type 2 diabetes. Prevalence of type 2 diabetes which wasabout2% in early 70s has sharply risen to more than 8% in late 90s and more than 14% in recent surveys in urban areas of our country. As per the latest prevalence study done by ICMR in 2011, India has 62.4 million diabetics and 72.2 million prediabetes.

Prevalence rate of type2 diabetes correlate with the degree of modernization and many societies which are rapidly undergoing a transformation from traditional to modern lifestyle are experiencing some of the highest rate of diabetes. Over the years, epidemiological studies done indifferent parts of the globe has shown that the Indian migrants settled abroad has a higher prevalence as compared to the local host population living in identical environment as well as the population native in India. This has been reported from countries with long established Indian population such as Singapore, Fiji islands, South Africa, Tanzania, Uganda, Trinidad and UK. Data generated over last two decades from our country have proved that the prevalence of type2 diabetes rapidly rising among urban population and is approaching the prevalence rates seen in the migrant Indian population.

While there is a drastic increase in prevalence rate in urban India, the prevalence in rural India has increased at slower rate. Consumption of traditional diet and relative absence of mechanization have protected the rural population. However as per recent survey done in Tamilnadu, prevalence of diabetes is rapidly rising even in rural areas. In PODIS study by Mohan and his group, prevalence of type 2 diabetes was 4.26% in rural areas. Another very worrisome finding is reduction in prevalence rate of impaired glucose tolerance (prediabetes). It means faster conversion of these people to diabetes and thus more rapid rise in prevalence of diabetes.

However as per recent study done by ICMR in 2011, in the states of Tamilnadu, Maharashtra, Jharkhand and in the city of Chandigarh, India already has 62.4 million people with diabetes, thus we are likely to surpass the figure of 79.4million much before the year of 2030.

There is a large variation in prevalence of type 2 diabetes between the communities. The highest rates are found in some native American tribes such as Pima Indians (over 50%),while low prevalence rates are found in least developed rural communities in many Afro-Asian countries(3%).

Gestational diabetes occurs in about 4% of pregnancies in the western world. In a study done in Chennai in 2003 the prevalence of GDM was 10.7% in rural and16.7% in urban areas. In the majority of cases, blood glucose returns to normal in postpartum period but the life time risk for future diabetes is substantially increased in women who develop GDM. About 40% develop diabetes in next 10 years.

The epidemics of interrelated lifestyle disorders have struck the globe like tsunami with its epicenter in rapidly developing and industrializing Asian continental India and China. A global epidemic of type 2 diabetes is occurring, particularly affecting developing countries and migrant population from these countries to more industrialized and westernized societies. This epidemic has closely followed the epidemic of obesity. The epidemic of type 2 diabetes itself is being closely followed by that of cardiovascular disorders particularly coronary artery disease. Until recently, based on the available epidemiological data, which was outdated to some extent, it was believed that India has a dubious distinction of having more diabetic patients than any other country including China. However, India is probably not the country with highest number of diabetics anymore. Recently(March 2010) a large scale epidemiological survey was done across China to study the prevalence of diabetes in that

country. Instead of using fasting plasma glucose as the sole test as done in early epidemiological studies, the survey also did post 75g glucose blood glucose levels in all the people who were included in the survey. It was found out that there are about93 million diabetic patients in China. Based on the earlier surveys it was estimated that china has about 39 million diabetic people, a figure lower than the estimated figure for prevalence of diabetics in India. However with 2011 data from ICMR study, we now know that the difference between the Chinese diabetic population based on the recent data and the Indian diabetic population is smaller.

As estimation of post glucose load blood glucose level is cumbersome and time consuming, Most of the epidemiological studies use fasting plasma glucose which is a bit less sensitive as compared to post 75 g glucose load plasma glucose level. However if a scientific national survey is done in our country using same methods of diagnosis of diabetes as used in the recent study in China, the prevalence of diabetes is likely to be much higher.

CLASSIFICATION

Diabetes mellitus fall into two major etiopathogenic category type 1 and type two diabetes. Diabetes can also develop secondary to other causes like genetic defects in beta cell functions, genetic defects in insulin action, diseases of exocrine pancreas or intake of certain drugs.

Onset of type 1 diabetes is usually in childhood and very acute. The patients with insulin dependent diabetes mellitus depend on insulin for their survival and withdrawal of insulin lead to ketoacidosis. Autoimmune or idiopathic destruction of insulin producing beta cells in Istets of Langerhans result in decreased endogenous insulin production vital for glycemic control and other metabolic function. Initial presentation of type 1 diabetes is usually dramatic with severe symptoms of polyuria, polydipsia, polyphagia,weightloss and in some cases diabetic ketoacidosis with symptoms of vomiting, deep rapid breathing characteristic of acidosis and deteriorating level of consciousness. Type 1 diabetes usually present in childhood and in young adults. Occasionally middle age people present with type 1 diabetes in some middle aged patients first presentation of type 1 diabetes is similar to type 2 which is more common in this age group.

In the early stages the may show response to oral hypoglycemic agents and are labelled wrongly as type 2 patients. However they become insulin dependent over a shorter period when compared to an average type 2 diabetic patient. These patients are positive for GAD antibodies confirming type 1 diabetes. These patients are labeled LADA[latent autoimmune diabetes in adults].

Type 2 diabetes the most common type all over the world, was labeled non-insulin dependent diabetes in the nineties. In type 2 diabetes environmental and genetic factors interplay leading to a chain of events ultimately leading to diabetes .most patients have varying degrees of dual defects, beta cell dysfunction and insulin resistance . Acquired insulin resistance can be multifactorial. Stress, drugs, sedentary life style are a few of the factors leading to acquired insulin resistance.

Secondary diabetes or other specific types of diabetes that are related to other specific disease process or genetic disorder[19],[20]. Secondary diabetes represent includes a variety of condition because of a recognized underlying pathology, a well-defined hyperglycemia governing molecular defect and or a clear association of a well-defined clinical syndrome and diabetes. This category of secondary diabetes

consist of genetic disorders of beta cell function and the insulin action , inflammatory infiltrative and neoplastic diseases of pancreas, endocrinopathies and infectious diseases leading to diabetes or certain medication and chemical exposure and rare forms of immune mediated diabetes and a variety of congenital syndromes associated hyperglycemia.

Maturity onset diabetes of the young [MODY] is a heterogeneous group of hyperglycemic disorder inherited in an autosomal dominant manner .MODY patients are usually not obese and only mildly hyperglycemic. Ketoacidosis is usually not seen the disorder is mild in nature and mask the clinical disorder for many years. Typically the disease occurs before 25 of age in childhood or adolescents. A strong family history of diabetes in multiple generation is usually present. Primary defects in beta cell function is responsible for all cases of MODY. MODY is numbered one through six according to the six separate genetic mutation

MODY 2 is characterized by mutation in the gene encoding the glycolytic enzyme, glucokinase. In MODY 1 hepatocyte nuclear factor 4 alpha , in MODY 3 hepatocyte nuclear factor 1 alpha , in MODY 4 insulin promoter factor 1,in MODY 5 hepatocyte nuclear

factor 1 beta and in MODY 6 neurogenic differentiation factor 1 are the transcription factors encoded by the genes affected by the genetic defect in MODY[21]. The most prevalent of the group is MODY 3 and the next common is MODY 2.

Genetic defects in insulin action. The insulin molecule or its receptor abnormality are rare condition that can lead to diabetes in infancy. Leprechaunism is characterized by severe insulin resistance, intrauterine growth retardation, dysmorphic features and acanthosis nigricans. Type A insulin resistance with acanthosis nigricans, lipodystrophic diabetes, Rabson Mendenhall syndrome (dentaldysplasia, dystrophic nails, precocious puberty) are the other forms of diabetes in under the category of genetic defects in insulin action. Peroxisome proliferator activated receptor gamma is associated with severe insulin resistance and diabetes.

Acute and chronic pancreatitis, hemochromatosis and cystic fibrosis can affect the parenchymal tissue of pancreas and can cause diabetes in later life. Malnutrition related fibrocalculous pancreatitis and carcinoma of pancreas is linked to diabetes

A number of medication has been related to the development of diabetes. Drugs associated with insulin resistance include

glucocorticoids, levothyroxine, atypical antipsychotics. Beta adrenergic antagonist, thiazide diuretics, calcium channel blockers and octreotide are agents that decrease insulin secretion. Beta cell destruction may be caused by rodenticide, vacor. Viral agents like rubella, mumps, coxsackie and adenovirus may produce immune response leading to type 1 diabetes. Stiffman syndrome with high anti-GAD antibody titers and diabetes is an autoimmune mediated condition. in congenital syndromes like Down' s syndrome Klinfelter's syndrome, Friedrich's ataxia ,Turner's syndrome, Prader-Willi syndrome, myotonic dystrophy, Wolfram'ssyndrome, Porphyria, Laurence Moon Beidl syndrome, diabetes is recorded with increased frequency.

Diabetes first diagnosed during pregnancy is termed gestational diabetes. It occurs in about 2 to 5 % of all pregnancies. Gestational diabetes results from insulin resistance of pregnancy interacting with beta cell defect. Usually blood glucose is normalized after delivery. Since significant insulin resistance of pregnancy develops only in third trimester, gestational diabetes sets in only in this period .presence of glucose intolerance in early pregnancy indicates preexisting type 1 or type 2 diabetes. Women having gestational diabetes are at higher risk to develop type 2 diabetes during later part of their life.

DIAGNOSIS OF DIABETES[22]

Criteria for Diabetes Diagnosis
HbA1C ≥6.5% Perform in lab using NGSP-certified method and standardized to DCCT assay
FBS ≥126 mg/dL Fasting defined as no caloric intake for ≥8 hrs
2-hr PG ≥200 mg/dLduring OGTT (75-g)
Random PG ≥200 mg/dL In persons with symptoms of hyperglycemia or hyperglycemic crisis
In the absence of unequivocal hyperglycemia results should be confirmed using repeat testing

HISTORY OF HbA1C

Gabbay et al.,in 1976 suggested measurement of glycosylated hemoglobin as an diabetic control.

Allan et al., in 1958, described a group of minor hemoglobins that can be separated from HbA1C,the major hemoglobin by ion exchange chromatography. These minor hemoglobins were designated as HbA1A,HbA1B and HbA1C – collectively called HbA1(a+b+c) or HbA1, the so called glycosylated hemoglobin

Increased levels of glycosylated hemoglobin was observed by Huismann Dozy in diabetic patients in 1992.

In 1975 it was demonstrated by Flucckinger and Winterhalter that HbA could be formed in vitro, by incubating either whole blood or purified hemoglobin at 37 degree celcius in the presence of hemoglobin. The relation between blood sugar and HbA1c was demonstrated by Koenig and Cerami in 1975. In 1976 Tattersal et al. in their twin study observed that metabolic abnormality led to an increased level of HbA1C in diabetes rather than a genetic marker. In 1993 DCCT trial observed a relation between type1 diabetes and HbA1C in 1998 UKPDS trial established the relationship between

type2 diabetes and HbA1C. In2010 ADA recommended HbA1C in the diagnosis of diabetes and pre-diabetes.

Hemoglobin A constitutes 90% hemoglobin of children more than six months of age and adults.HbA1C is the most abundant of the minor hemoglobin components, that is separated when HbA is passed through a chromatographic column. Except for the hexose group linked to the N terminal amino acid of the beta chain, the HbA1C is structurally similar to HbA. This is called the glycosylated hemoglobin. Normal value of HbA1C dependents on the methodology used and also varies from lab to lab.

Structure and biosynthesis

Post-translational, non-enzymatic slow glycosylation of HbA within the RBC leads to the synthesis of HbA1C which occurs throughout the life span of hemoglobin in circulation that is around 120 days.HbA1C is formed in a two stage process. The first stage includes the formation of a week attachment between the amino group of HbA and glucose by a Schiff base. This is called pre-HbA1C. In the second stage an Amadori reaction takes place which leads to a molecular rearrangement of aldamin which leads to the formation of ketamine in which glucose molecule is attached to hemoglobin forming HbA1C.

The preHbA1C stage seems to be rapid and reversible whereas HbA1C,the second stage is slow and irreversible[23],[24],[25].

FIGURE1: STRUCTURE OF HEMOGLOBIN A1C

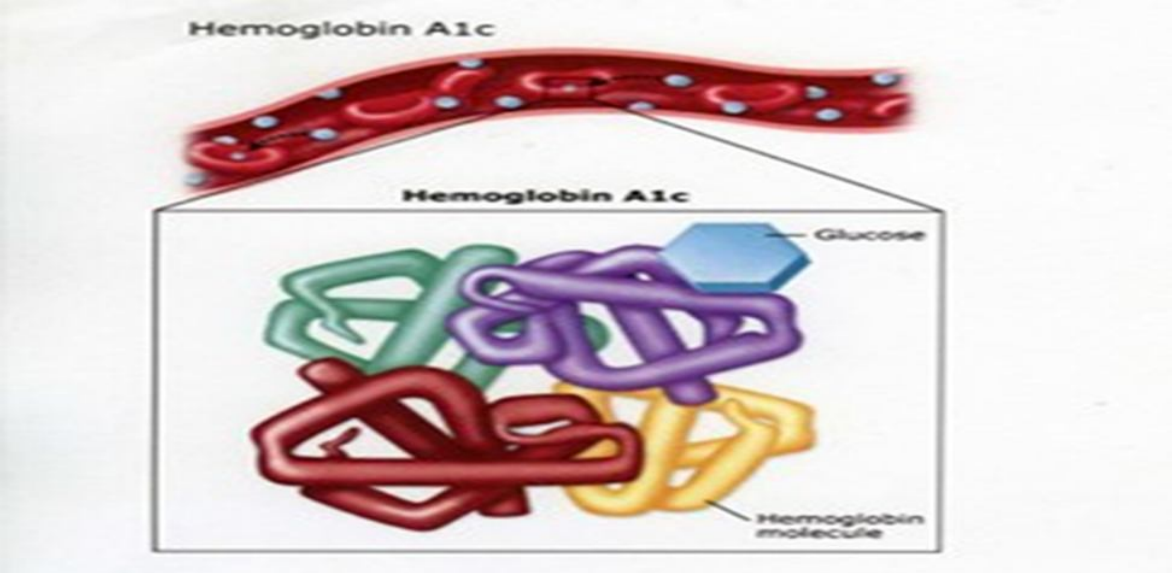


FIGURE 2 : N TERMINUS OF BETA CHAIN

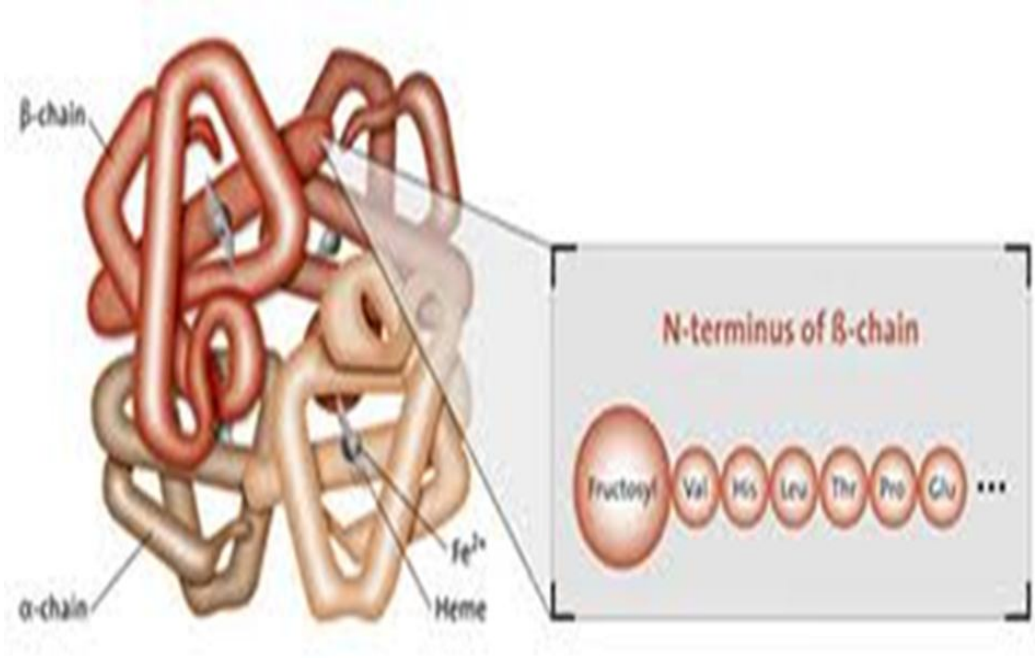
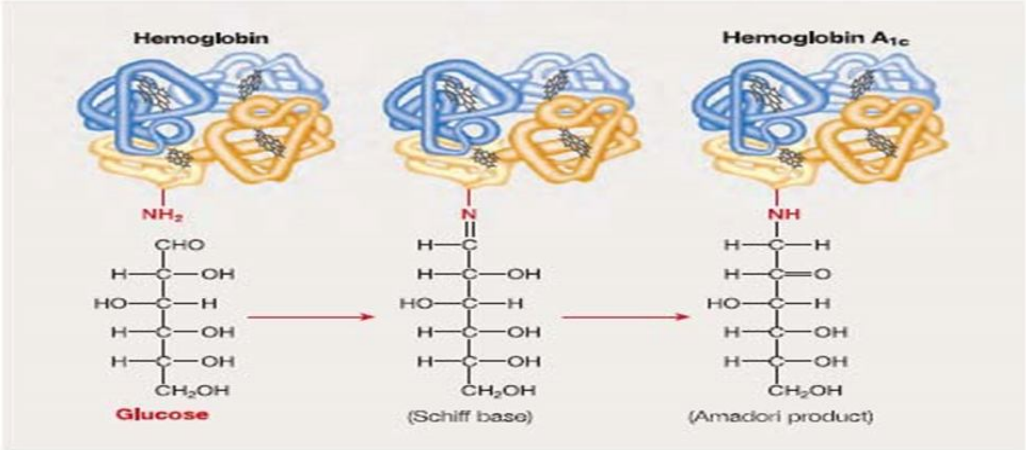


FIGURE 3 : FORMATION OF HbA1C



HbA1C is formed slowly and almost irreversibly by the condensation of glucose and Hb in RBC. With simultaneous accumulation of HbA1C it is evident that the amount of HbA1C should be a reflection of average glucose concentration seen by the RBC's during their life span.

1% of HbA1C was reported to represent 35mg % of blood glucose levels by Goldstein in 1984[26]. Similarly a formula was derived from univariate analysis by Svendesen et al. In 1982 such as HbA1C=2.07 X [mean blood glucose]0.596. These formulas are not for general use because of methodology differences and acute fluctuations in blood glucose.

When properly assayed HbA1C% provides a good cumulative index of glycemic control for a preceding period of 3 months.

Glucose in HbA1C gets attached to the beta chain of HbA to its N terminal which is also as site for 2,3 Diphosphoglycerate [2,3DPG],which is the regulator of hemoglobin function . High affinity for oxygen is seen in HbA1C. Therefore in diabetes with increased glycated hemoglobin and relative deficiency of 2,3 DPG can result in decreased oxygenation of tissues .this forms one of the pathogenic hypothesis of microvascular complication including retinopathy[27].

Advantages of HbA1C ESTIMATION

1. It's a simple procedure.
2. No need for dietary preparation.
3. It eliminates the variability noted with glucose tolerance test.
4. There is a reasonably accurate reflection of overall chronic hyperglycemia.
5. Duration of diabetes, weight and sex does not affect HbA1C levels.

Disadvantages of HbA1C estimation

1. The rate of formation of glycosylation is much faster than its disappearance.
2. Results dependent on methods used
3. No internationally accepted standard is not available yet.

Conditions leading to false elevation of HbA1C.

A. Chromatographic abnormalities
    1. Hyperlipidemia [due to lactescence]
    2. Elevated temperature and or buffer Ph.
    3. Negatively charged Hb variants ,such as HbF
    4. Acute hyperglycemia[fast glycosylation]
B. Other posttranslational modification of hemoglobin
    1. Aspirin[acetylation]
    2. Antibiotics[penicilloylation]
    3. Alcohol[5-deoxy-xylulose-l-PO4]
    4. Uremia [carbamylation]

Conditions leading to falsely low HbA1C levels

A. Chromatographic abnormalities
    1. Low temperature and or buffer Ph.
    2. Positively charged Hb variants such as, Hb S or HbC.

B. Altered RBC dynamics

1. Increased destruction of RBCs-hemolytic anemia

2. Active erythropoiesis as in pregnancy

3. Recent blood transfusion.

Conditions leading to falsely high values of HbA1C

1. Iron deficiency anemia
2. Vitamin B12 deficiency
3. Folate deficiency

Methods for measuring glycosylated hemoglobin[28]

1. Chromatographic methods[Kynoch and Lehmann]
2. Colorimetric method[Fluckiger and Winterhalter]
3. Radioimmuno assay ,

In the 1990s, after the publication of the DCCT trials the American diabetes association began to make treatment recommendations on the basis of HbA1C. Presently HbA1C has become the gold standard for diabetic management in both clinical and research settings[29].The ADA recommends HbA1C less than 7% as the glycemic control goal.

Platelets are small anuclear cell important in haemostasis and thrombosis[30].In 1841 Addison described platelets as extremely minute granules in clotted blood. Bizzozero coined the term platelets and observed there adhesive quality with increased stickiness once vessel wall is damaged platelets have a characteristic discoid shape and are formed from the cytoplasm of megakaryocytes younger platelets have more functional ability .10 3 to 10 11 platelets are formed by each megakaryocytes

Platelet formation

Megakaryocytes residing primarily in the bone marrow,also found in lung and peripheral blood are rare myeloid cells which constitute less than 1 % of the myeloid cells. In early development, megakaryopoiesis occurs in the yolk sac and the fetal liver. The pluripotent stem cells megakaryocytes develop into two types of precursors, burst forming cells and colony forming cells. CD34 antigen is expressed on both the types of megakaryocytic precursors[31]. Thrombopoiesis is primarily regulated by the cytokine, thrombopoietin, to maintain a constant platelet mass. Thrombopoietin is thought to act along with other factors like IL-3,IL-6 and IL-11 although they are not essential for megakaryocytes maturation.

The platelets were identified over 120 years ago but the mechanism of platelet genesis has not attained a consensus .A modified flow model of platelet formation has been recently supported by evidences. In this model, proplatelets, an intermediate pseudopodial extentions are essential in platelet formation. Proplatelets are formed by evagination of the mature megakaryocyte's extensive internal membrane system .this concept was first introduced by Wright in 1906 where he describes platelet detachment from megakaryocytes pseudopods. The platelet formation from megakaryocytes involves the conversion of the cytoplasm into 100 to 500 micrometer long branched proplatelets over which individual platelets are formed. Generally a single site on megacaryocytes one or more pseudopodia develops forming proplatelet and then platelets. About 4 to 10 hours the pseudopodia continuously elongate and taper into proplatelets of an average diameter of 2 to 4 micrometer. Further proplatelet generation continuous at or near the initial site of proplatelet formation and in a wave like manner spreads throughout the rest of the cell till the cytoplasm of the megakaryocytes is completely converted into a complex and extensive network of interconnected proplatelets. The megakaryocytes cell body with multilobed nucleaus is compressed into a central mass without cytoplasm and ultimately extruded and

degraded .The events involved in platelet formation from proplatelets have not been identified precisely.

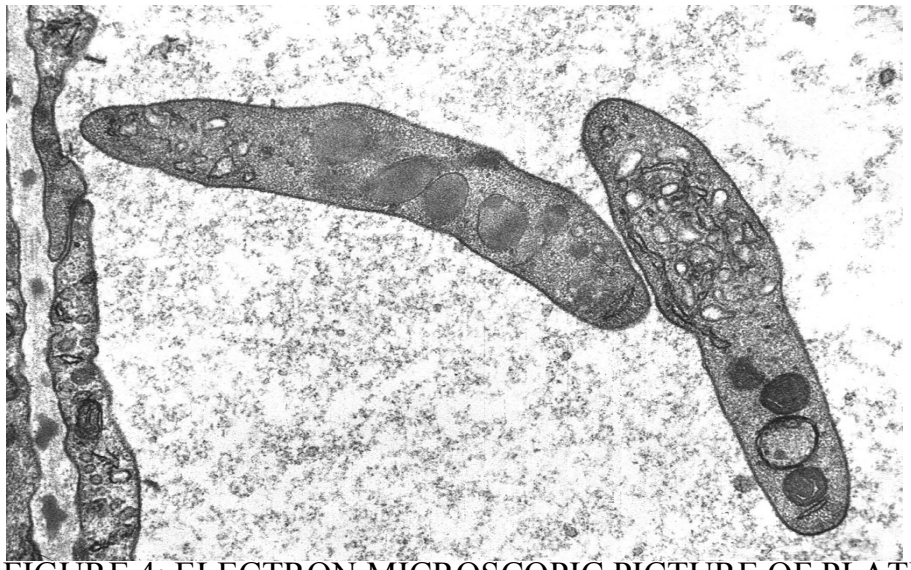


FIGURE 4: ELECTRON MICROSCOPIC PICTURE OF PLATELET

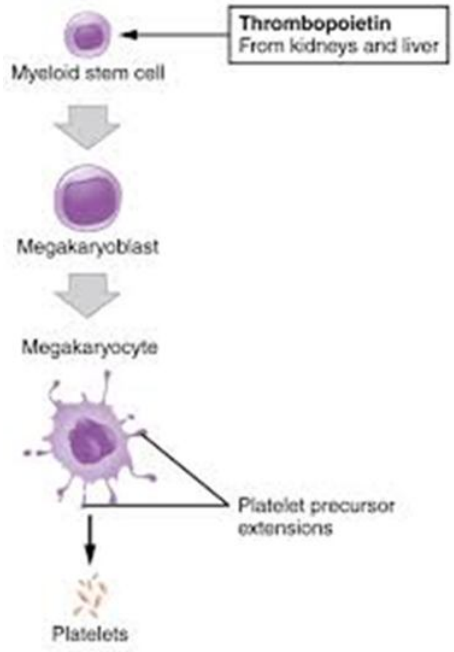


FIGURE 5: PLATELET FORMATION

Platelets have an average life span of 7 to 10 days. Platelets are removed from circulation mainly by two mechanism, firstly by senescence or by an endothelial supportive function of random removal of fixed fraction of platelets of about 7.1 * 10 9 per liter per day. Splenic macrophages primarily remove the senescent platelets. Hepaticmacrophages quickly remove severely damaged platelets because of the larger blood flow through the liver[32]. Accumulation of surface IgG is assumed in aging platelets containing decreased levels of sialic acid [33].

Wright –stained smears reveal platelets to be small, anuclear measuring about 2 micrometer diameter and 8 fl volume approximately[34],[35].

Platelets exist in resting and activated forms. The activated form results from agonist stimulation [i.e., response to thrombin]. The resting state form has a base line metabolic activity. Most information on platelet anatomy is derived from transmission electron microscopy. The platelet structure is classified into four, the platelet surface, membrane structures, cytoskeleton and granules[36].

The platelet plasma membrane, a typical 20 mm thick trilaminar structure which separates extra cellular and intra cellular regions[37] .

Although the platelet plasma membrane appears similar to that of other blood cells, the platelet membrane is complex in composition, function and distribution. The phospholipid bilayer of the platelet membrane incorporates a number of glycoprotein and lipids. This helps the membrane in integrating a variety of intra and extra platelet evens like permeability, platelet adhesion, aggregation and agonist stimulation.

Glycocalyx, a 15-20 mm thick, layer of lipid, sugars and proteins covers the outer surface of platelet plasma membrane. The platelet glycocalyx coats the surface connected canalicular system and interacts with both cellular and plasma components of blood and blood vessels. The platelet glycocalyx provides a transfer point by endocytosis for plasmaprotein such as fibrinogen[38],[39].The platelet glycocalyx contains glycolipids, absorbed plasma proteins ,glycolipids , mucopolysaccharides [40],[41]. The glycocalyx has anet negative charge mainly due tosialic acid residues oncertainproteins like gp1. This negative charge is considered to be the reason tominimize the attachment of circulating platelets to each other and to the vessel wall.

Platelets have a high content of actin and their contractile response during activation relates it to be like muscle cell .muscle like properties are seen in two membranous system of platelets , dense

tubular system and surface connected canalicular system, resembling sarcotubules and transverse tubules , respectively[42].

The shape of the platelet and its ability to contract and spread is determined by cytoskeleton which is constituted by a cytoplasmic framework of monomers, tubules and filaments[43].platelets change their shape and produce extracellular extensions and collect and extrude secretory granules thus affecting surface activity .the varied functions of platelets are performed by 3 separate structures membrane skeleton covering the plasma membranes in a surface ,the actin and intermediate filaments also called solgel zone which fills the cytoplasm ,and finally circumferential microtubule encircling the platelets and produce the resting disc-like form[44].

Normally platelet function require an amplified or accentuated stimulus to get an appropriate response .this purpose is served by the secretory granules which release of additional stimulatory materials which are previously stored within the resting platelet. The dense bodies and the alpha granules appears to be the two main secretory granules with their highly reactive readily available contents like adenosine diphosphate and fibrinogen [45].platelet metabolic activity dramatically increased once the platelet granule secretion begins. A

wave of calcium released and is marked by increased adenosin triphosphate production[46],[47].

Small granules 90nm in diameter, demonstrable with alkaline diaminobenzidine due to their catalase activity are the microperoxisome [48].the microperoxisomes may participate in the synthesis of platelet activating factor. The ultimate fate of the microperoxisomes in the platelet cytoplasm is not known[49].platelet organelles, distinguished by electron dense bristle coat are coated vesicles of 70 to 90 nm diameter. The surface coat is formed by clathrin .the special staining reveals that the same polyhedral surface coat is same as that in the plasma and the surface connected cannalicular membrane found on the coated pits and vesicles[50]. The platelet mitochondria are smaller in size otherwise similar to those in all other types. There are approximately seven per human platelet. They serve as the action site for respiratory chain and citric acid cycle[51]. Glycogen plays an important role in platelet metabolism and is found in small particles or masses of closely associated particles[52].

There are various functions of platelets which include adhesion, aggregation, secretion, clot retraction and procoagulant activity .vascular damage leads to the exposure of subendothelial matrix

protein which initiates platelet adhesion. The rate of shear affect the platelet glycoprotein receptor which mediates adhesion. Recruitment of circulating platelets into thrombus is also a part of adhesion[53].

The platelets when activated attains spherical shape and extend psueudopodia which enable them to attach to other platelets and vessel wall. The spherical transition increases the platelets optical density. The shape change occurs as a consequence of increased intracellular calcium ions which activates myosin light chain kinase or by inhibition of myosin light chain phosphatase mediating phosphorylation of myosin light chain, which is regulated down stream of Rho kinase.

The cross linking of platelets through fibrinogen binding , or other bivalent or multivalent ligands like vWF to the integrin alpha 2b beta3 on adjacent

The different type of granules contains distinct contents that display varied roles in hemostasis. The dense or alpha granule deficiency is the basis of secretory disorders associated with excessive bleeding.

The assembly of two multiprotein complex, namely the tenase and prothrombinase complexes play a vital role in coagulation cascade and

provide a negatively charged phospholipid surface an important function, thus enabling platelet activation for its critical function. Procoagulant activity is described as the formation of negatively charged lipids surface on activated platelets. This is formed by phosphatidyl serine movement to the outer leaflet from the inner of the platelet membrane.

Platelet activation leads to the generation of platelet derived microparticles seen together with an increase in procoagulant activities. Calcium entry is required for the formation of platelet micromolecules and is seen in response to stimulation by calcium ionophore which requires high agonist concentrations and favorable conditions for them to be formed upon receptor activation.

Clot retraction: it is a known fact for more than 2 centuries over a time course to minute to hours blood clot retracts. This clot retraction helps the platelet rich thrombus to withstand high shear forces found in small arterioles and other vessels. After addition of thrombin, thrombin –stimulated platelet rich plasma can be measured readily for clot retraction.

The peripheral blood quantification of platelet count is a well-recognized tool. Several indices have been derived from platelets the

most common of them being platelet distribution width and mean platelet volume. Platelet parameters like, mean platelet volume[MPV], platelet distribution width [PDW],plateletcrit [PCT], platelet to large cell ratio [PLCR],can be measured by the use recent advanced automated blood cell analyzers. These measurements provide some important information but are not yet accepted for routine clinical use[54].

MEAN PLATELET VOLUME[MPV]

Peripheral blood platelet counts does not reveal much about platelet related haemostatic function unless there is a severely low platelet count. But most automated blood analyzers measure an important platelet parameter, the mean platelet volume which is a clinically useful pathophysiological information on vascular diseases of a patient[55].

PHYSIOLOGY OF PLATELET SIZE

Mean platelet volume appears to be a determinant or a marker of platelet function. In vitro large platelets are more reactive when compared to small platelets. The larger platelets aggregate more rapidly to platelet agonist such as adenosine diphosphate, collagen and adrenaline lead to production of vasoactive factors such as arachidonic

acid metabolites, serotonin, adenosine triphosphate and beta thromboglobulin. The large platelets have high LDH activity and contains more dense granules. They are associated with a decreased bleeding time[56].

MEAN PLATELET VOLUME IN DIABETES

Mean platelet volume is related to platelet aggregation, both in whole blood and in platelet rich plasma, in population in some subjects or some disease state like diabetes, heart diseases. Increased levels of adhesion molecules like Pselectin,glycoprotein2b 3a has been recognized in large platelets although the surface density of the glycoprotein is usually constant and is not affected by the platelet volume.

Platelets, anucleate cells, have no protein synthetic capacity. Platelets are heterogeneous with regard to their hemostatic potential, density and size. It was believed that platelet size decreased with age. The recent evidences favor the platelet precursor cell, the MK, determine the mean platelet volume and other parameters, protein content and reactivity at or before thrombopoiesis. Among the mammalian cells MK's are unique in that they are polyploid. This means that the MK cells can double their DNA content by a process

termed endomitosis without a full mitotic cell division. MK's produce a population of cells whose ploidy range from 4N to 128N,(2N represents normal diploid state) undergoing a varying number of endomitotic division. The model ploidy in the majority of mammal studied 16N is the most common studied till date .each MK cell produce about 1000 to 2000 platelets probably by cytoplasmic fragmentation of MK's in pulmonary circulation . MK and platelets are considered a single system by the name, the megakaryocyte-platelet hemostatic axis[MPHA]. In normal population the platelet count is inversely proportional to mean platelet volume, the product of mean platelet volume and platelet count is a near constant – called platelet mass, platelet mass is related to bleeding time and bleeding time is inversely proportional to MK size and ploidy . In the absence of platelet production, when acute platelet destruction occurs the MK ploidy remains unaffected whereas mean platelet volume increased .When platelet production and destruction occurs at the same time both mean platelet volume and MK ploidy increases. When platelet production along is increased MK ploidy is increased. This leads to the postulation that regulation of MK ploidy and hence platelet count and mean platelet volume are under different hormonal control. Variations in MK ploidy and size and cytoplasmic volume are related to the

change in platelet production whereas variation in mean platelet volume results from a change in the platelet destruction rate.

The ideal method for measuring the volume of platelet utilizes the changes in light diffractions and electrical impedance when platelet pass through a narrow aperture. In Coulter hematology analyzers electrical impedance method is used whereas light diffraction is used by technicon. Semi-quantitative measurements of diameter of platelets on platelet smears or using flow cytometry are less satisfactory methods to measure platelet volume.

In coulter series a voltage change is created proportional to the particle size when the cells held in fluid suspension are flown through a small aperture. A raw histogram is generated and a log-normal curve is fitted to the data .using numerical integration platelet count and mean platelet volume is calculated[57].in the Sysmex measures cells in fluid suspensions, similar to Coulter series although in addition cells are hydro-dynamically focused so that cells travel in a straight line through the aperture. This prevents spurious changes in electrical field caused by the cells flowing throw at the edge of the aperture. It defers from coulter also because the upper and lower discriminators are both mobile. The distribution curve obtained is not a fitted curve but an

actual data. the formula used to calculate mean platelet volume is [MPV(fl)=Pct(%)*1000/Plt(10^3/microliter).the laser –optic technology is used to measure the granularity and size of cells in suspension by the Technicon instruments. In this method a beam of light is passed through the cells and sides scatter is proportional to density or granularity and forward scatter is proportional to the size of particles . mean platelet volume is calculated as the mean after the data is plotted on a platelet histogram.

A cross sectional study was conducted by Dow university of health science Karachi Pakistan by Zuberi B F et al in 2006-07[58].

Diabetes mellitus is a prothrombotic state with increased activation of platelets and coagulation proteins and decreased fibrinolytic activity [59].the differences in platelet

Function in diabetic and non-diabetic population is called diabetic thrombocytopathy. Enhanced platelet aggregation is seen in diabetic patients in the early course of disease. Certain abnormal features exhibited by the platelets of diabetic patients make them more prone to thrombotic episodes [60]

Enhanced Platelet activation

The in vivo activation of circulating platelets in diabetic individuals have been studied widely[61].Most reports hypothesise a specific priming of hyper sensitive platelets in diabetics in response to platelet agonists. More frequent episodes of release of their granules occurs in circulating platelets. Platelet survival is reduced due to their accelerated sequestration in the circulation implied by augmented granule release. Increased thrombopoiesis is reflected by the increased platelet turnover in diabetic patients.[62],[63]

Altered response to agonists, increased fibrinogen binding, enhanced glycoprotein receptors expression, decreased membrane fluidity, and increase in adhesive proteins on the platelet surface is instrumental in platelet activation.

Platelets hyper-aggregability

Glucose responsive platelets hyper aggregation was recognized in 1965.[64] When compared to non-diabetic individuals, diabetics exhibit an enhanced platelet aggregation in response to thrombin, collagen, arachidonic acid epinephrine and adenosine diphosphate[65]. After stimulation with platelet agonists these platelets show reduced

threshold for platelet aggregation under in vitro conditions.[66]In diabetic patients associated with macro vascular disease, increased platelet aggregation is more apparent.[67] Increased adhesiveness and increased spontaneous aggregation and also increased aggregation on extra cellular matrix is seen in platelets of diabetic individuals.

Increased arachidonic acid metabolism

Thromboxane A2 is one of the most potent of platelet activators. Accelerated calcium mobilization occurs as a result increased protein phosphorylation, enhanced inositol triphosphate production which itself results from an enhanced activation of arachidonic acid pathway leads to increased thromboxane A2 formation, and increased phosphoinositide turnover resulting in increased protein phosphorylation[68].

Increased Thromboxane A2 production has been reported in both in vitro and in vivo conditions in diabetic patients. Increased TXA2 synthesis in vitro is noted when platelet agonist is added to platelet rich plasma[69]. Increased thromboxane metabolism in vivo is supported by the presence of increased urinary excretion of 11-dehydro-ThromboxaneB2[70],[71].

Thromboxane metabolism is directly affected by plasma glucose concentration and HbA1c. Reduced thromboxane A2 production has been identified in several studies with improved glycemic control but not in all studies[72],[73]. Micro and macro angiopathy associated with diabetes has been related to increased production of thromboxane A2.

Increased calcium flux

Abnormal calcium homeostasis is exhibited by the Platelets of patients with type 2 diabetes mellitus. High levels of intracellular free calcium is seen in patients with diabetes mellitus along with increased calcium mobilization from intra-platelet storage pool[74],[75]. The decreased membrane fluidity is attributed to the free intracellular calcium. Altered properties of platelet membranes in platelet hyper function is correlated to calcium mobilization.[76]Intracellular magnesium concentrations are reduced along with alterations in platelet calcium homeostasis consistent with an increase in platelet adhesiveness and hyperaggregability.[77]

Platelets nitric oxide synthesis

Platelet endothelium interactions and endothelium mediated vasodilatation is inhibited by Nitric oxide (NO) and prostacyclin. In Diabetic patients platelets

NO and prostacyclin production is decreased. Concentration of NO is decreased in the platelets of diabetic patients when compared to non-diabetic individuals.[78]NO synthesis in platelets is stimulated by insulin.[79]

Platelet secretary products

Mitogenic and chemotactic factors like platelet-derived growth factor, transforming growth factor-β , vascular endothelial growth factor, basic fibroblast growth factor ,platelet derived epidermal growth factor (PDEGF) and insulin-like growth factor-1 (IGF-1) are released by activated platelet. Platelet factor-4 (PF-4), plasminogen activator inhibitor-1 (PAI-1), von Willebrand factor, β-thromboglobulin, fibrinogen, fibronectin and thrombospondin are also significantly released upon platelet activation.[80] Elevated plasma levels of thromboglobulin and Platelet factor 4 is in patients with diabetes mellitus.[81]

Platelet membrane glycation

The non-enzymatic glycation of platelet membrane proteins is affected by hyperglycemia. This Non-enzymatic glycation of platelet membrane proteins produces alterations in the protein structure, conformation and membrane lipid dynamics.[82],[83],[84] Reduced platelet membrane fluidity also seems to be related to the extent of glycation of membrane proteins. Enhanced expression of receptors results from altered dynamics of platelet membrane lipids thus affecting the platelet functions. The receptors whose expression is enhanced includes Pselectin,fibrinogen receptors and von Willebrand factor receptors.[85],[86]The increased expression of adhesion receptors, like, alpha2beta3 ,results in frequent episodes of platelet activation and degranulation. Increased expression of these adhesion receptors makes the platelets more susceptible topotential ligands.[87]

Membrane glycation of low density lipoproteins

Low density lipoproteins (LDL) glycation has been shown to increase platelet sensitivity to aggregating agents.[88]The degree of low density lipoprotein glycation is proportional to the rate of platelet aggregation.Increase in non-enzymatically glycated is caused by hyperglycaemia which in turn renders the platelets more susceptible to

oxidative stress.[89],[90]Non-enzymatically Glycated LDL inhibits platelet membrane Calcium ATPase which results in increased intracellular Calcium concentration and decreased nitric oxide synthase activity.[91]Glycated LDL leads to inhibition of platelet membrane Na+/K+- adenosine triphosphatase activity is and result in platelet dysfunction.[92] Lipoproteins also increase thromboxane generation during platelet activation.[93]The activation of prothrombinase complex in diabetes mellitus is increased by oxidized lipids by providing a surface for activation.

Expression of increased surface markers on platelet membrane

Several platelet specific glycoprotein receptors are increased in number, adhesiveness and activity in diabetic patients. In diabetic patients an increased level of GPIIb/IIIa (αIIbβ3), GPIb-IX-V, GPIa/IIa, CD62 and CD63 have been observed[94],[95],[96]. Increased expression of platelet αIIbβ3 is consistent with enhanced fibrinogen binding and aggregability in patients with diabetes.[97]Platelet receptor activation has been correlated with glycaemia and also with vascular complications.[98]Enhanced surface expression of these adhesion molecules suggests that platelets also communicate with leukocytes. Platelets play an important role in inflammation mediated tissue

damage in the vessels. In diabetic patients an up-regulation ofCD40-CD40 ligand system has been observed.[99]CD40Ligand levels on platelets corresponds with the high HbA1c levels. P-selectin and CD40Ligand are shed into plasma in biologically active soluble form from the platelet surface .[100],[101] Increased levels of soluble P-selectin and CD40Ligand are seen in patients with diabetes mellitus and cardiovascular diseases.[102],[103],[104] Elevated levels of these compounds may reflect a prothrombotic state and also accelerated atherosclerosis.[105],[106],[107]

Hypersensitivity to collagen is exhibited by platelets of patients with diabetes mellitus. Increased collagen-induced aggregation correlates with the elevated expression of platelet Fc-receptor.[108],[109]

Platelet metabolic alterations

Glucose entry into the platelets is not dependent on insulin,therefore intra-platelet glucose concentration reflects the extra cellular glucose concentration.[110]Hyperglycaemia is a definite causal factor for in vivo platelet activation and platelet hyperactivity in diabetic patients.[111]

Hyperglycaemia induces an increased activation of platelets exposed to high shear stress both in vitro and in vivo.[112] Impaired calcium homeostasis, activation of PKC, decreased production of platelet-derived nitric acid and increased formation of superoxide anion leads to increased sensitivity to agonists and metabolic alterations of platelets. Reduced glutathione levels and nitric oxide synthase activity are the few other metabolic alterations in the platelets diabetic patients.[113],[114]

Altered platelet size and volume

Predominantly large platelets circulate in the blood of diabetic patients. This is considered secondary to increased ploidy and activation of megakaryocytes.[115]Larger and younger platelets are considered to be more reactive.

Mean platelet volume (MPV) corresponds to the number of glycoprotein molecules on the platelet membrane, the thromboxane synthesizing capacity and platelet granule contents of various platelet specific protein.

Platelet life span

Platelet survival in patients with diabetes mellitus have produced conflicting results in various studies. Some studies show a decreased platelet survival in patients with diabetes mellitus with presence of vascular complications.[116]While a few studies did not find any difference in platelet survival and vascular complications with diabetes mellitus compared to normal healthy controls.[117]

Platelet-leukocyte interaction

Inflammation and thrombosis cause activation of endothelial cells, leukocytes and platelets. Complex interaction between these cells is influenced by several mediators.

Platelets may influence leukocyte activation, chemotaxis and phagocytosis. Platelet-released adenine nucleotides and platelet derived growth factor induce leukocyte degranulation. Adherent platelets, platelet-derived micro-particles, PDGF, PF-4 and TXA2 enhance leukocyte rolling and adhesion.65 PDGF is also a chemo attractant and enhances phagocytosis by neutrophils and monocytes. Superoxide formation by neutrophils may be enhanced by platelets bound to neutrophils or platelet-released ADP while intact non stimulated

platelets may inhibit neutrophil superoxide production.[118] Leukocyte chemotaxis, adhesion and superoxide generation are inhibited by P-selectin and nitric oxide released from platelets.[119]

Platelets and platelet-derived products influence leukocyte function in several ways. Platelets and leukocytes may form platelet-leukocyte aggregates or conjugates (PLAs) mainly via platelet-expressed Pselectin and its receptors P-selectin glycoprotein ligand- 1, CD15, αIIbβ3 and CD11b/CD18. Diabetic angiopathy involves atherosclerosis, inflammation and thrombosis due to abnormal function of platelet and leukocyte. In diabetic microangiopathy increased platelet and leukocyte activation and heterotypic aggregation are evident.[120]

MPV AND ANTIPLATELET DRUGS

Platelet aggregation is an essential step in physiological hemostasis and is involved in vascular pathology such as atherosclerosis, arterial thromboembolism, unstable angina pectoris, myocardial infarction, transient ischemic attacks and stroke[121].the inhibition of platelet aggregation, example by aspirin, has become an important treatment for unstable angina pectoris and transient ischemic attack and secondary prevention of myocardial infarction and stroke.

Aspirin inhibits platelet aggregation through an irreversible inhibition of the cyclooxygenase. It is not known whether this impairment of platelet function has an influence on the feedback control system of platelet production and hence on platelet count and platelet volume. Stephen Erhart et al studied the influence of aspirin on platelet count, volume and total platelet mass in vitro and in a randomized double blind placebo control in 20 healthy young male volunteers in vivo. The platelet count was unaffected by increasing concentrations of aspirin in vitro over 4 hours, indicating that there was no platelet destruction by aspirin even with the high concentration of 250 microgram per ml which is well above concentration reached in vivo usually. The platelet volume was unaffected by aspirin and remained constant over time. In vivo studies showed that repeated blood sampling during a seven day treatment with 250 mg aspirin daily showed an increased platelet count and total platelet mass. An increased platelet count and mass were also in the placebo group on day four. Because of this observation the study was repeated with a minimal volume taken only on day four. Surprisingly both aspirin and placebo had not effect under this condition. Therefore, they stated that aspirin treatment together with repeated small bleeding increased platelet count and mass, but not aspirin treatment by itself. Aspirin treatment without repeated blood

withdrawal had no effect. These data indicate that aspirin may affect the circulating platelet mass under certain conditions.

MPV AND AGE

It was used to be thought that the platelet size decreased with age, but more recent evidence suggest that MPV and other platelet parameters and therefore platelet protein content and reactivity, are determined primarily at or before thrombopoesis by the platelet precursor cell, the MK.

MPVAND GENDER

Gender dependent differences in platelet count have been demonstrated in few studies. In female patients platelet count is higher than in the male population, which seems to show the hormonal variations or an alternate mechanism associated with normal cycle. Anna M Butkiewicz et al[122]conducted a study on healthy blood donors divided into groups of the two gender. Platelet count and mean platelet volume were determined on a hematological analyzer. Higher platelet count was noted in the group of women as compared to men. At the same time women had lower thrombopoietin concentration compared to men. No statistically significant difference were found in the mean platelet volume, though there was a slight increase in females.

MPV AND HYPERTENSION

MPV a determinant of platelet function, is a recently found risk factor for atherothrombosis. Coban et al selected essential hypertensive patients, 36 white coat hypertensive subjects and 36 normotensive control subjects match for age, gender, and BMI. MPV was significantly higher in essential hypertensives and white coat hypertensives than in normotensives:it was also higher in essential hypertensives than in white coat hypertensives.[123] Platelet counts were not different among the study group. MPV was positively correlated with ambulatory diastolic blood pressure in essential hypertension and white coat hypertension group. Platelet size is also found to be elevated in individuals with hypertension and diabetes mellitus, both conditions that predispose to the development of vascular disease.

MPV AND METABOLIC SYNDROME

Giuseppe Lippi et al performed a retrospective analysis on the data base of the laboratory information system of the clinical chemistry laboratory in Italy. Data for MPV, blood glucose, lipid profile values were retrieved from all outpatients consecutively referred by a general practitioner for routine blood testing. Cumulative results for lipid profile, MPV, blood glucose were retrieved for two years. The mean

MPV of subjects with all biochemical markers suggestive of the metabolic syndrome was slightly higher but not significantly different from that of control subjects.

MPV AND SMOKING

Tobacco smoking is one of the major factors accelerates atherosclerosis. Deleterious effects of smoking are associated with generation of free radicals that breakdown nitric oxide, which on the one hand enhances thromboxane synthesis, but on the other reduces production of prostacyclin, thus leading to clotting disorders, additionally enhanced by increased production of fibrinogen and factor seven. Butkiewicz AM et al designed a study to assess platelet parameters in smoking healthy subjects with reference to sex. [124]All the subjects were tested for platelet count, MPV, percentage of large platelet, concentration of thromboglobulin,P selectin and thrombopoietin, percentage of reticulate platelet and absolute count of reticulated platelet. In neither of the sexes smoking had an effect on MPV, percentage of large platelets, concentration of thrombopoietin, absolute count of reticulate platelet and concentration of thromboglobulin.

MPV AND ISCHEMIC HEART DISEASE

A study done by MM Khandekr and AS Khurana et al on patients diagnosed with unstable angina or acute myocardial infarction diagnosed on the basis of history, characteristic of electrocardiographic changes and increased cardiac enzyme activities. MPV, platelet distribution width and platelet large cell ratio were significantly raised in patients with acute myocardial infarction and unstable angina. Larger platelets are hemostaticaly more active and a risk factor for developing coronary thrombosis, leading to myocardial infarction. Patients with larger platelets can easily be identified during routine hematological analysis and could possibly benefit from preventive treatment.[125]

MPV AND STROKE

In some pathologic condition the megakaryocyte platelet hemostatic axis is chronically or acutely perturbed resulting in the production of hyper functional platelets which may be involved in subsequent vascular disease or an acute thrombotic event such as stroke. There is evidence that platelet function is accentuated in acute ischemic stroke. Therefore, a fundamental is whether this increase in platelet reactivity precedes the stroke, and plays a part in initiating the

event, or represents a reactive change to it. The development of atherosclerosis involves local platelet adhesion, but whether widespread systematic activation of platelet is present is an open question. The study of MKs and platelets in acute stage within 36 hours of onset of stroke would yield valuable information on the subject. MPV measured at this stage may well reflect, at least in part, the potential reactivity of platelets prior to the stroke. However, the dynamics of platelet consumption and production in the acute phase of stroke are not yet understood well enough to rule out the possibility that MPV is being modified to some extent by the acute destruction of platelets and subsequent change in the fragmentation of MK cytoplasm. If MK parameters could be shown to the abnormal shortly following the stroke this would strongly suggest that the MPHA was chronically perturbed prior to the stroke[126]. Increased platelet function, and in some cases a shift in MK indices in a pro-thrombotic direction has been shown in stroke risk factors such as hypertension, hypercholesterolemia, diabetes mellitus and smoking and in vascular condition associated with stroke such as atherosclerosis, peripheral vascular disease and myocardial infarction. Thus it seem probable that in patients with certain risk factors profiles systemic platelet activation precedes the onset of stroke.

In a study done by O'malley et al mean platelet volume was found to be high in acute stroke. In addition, platelet count was reduced in stroke patients compared with control subjects. Repeated measurements of mean platelet volume and platelet count in available survivors showed no significant change from the acute phase. Platelet changes did not relate to outcome measured at six months. In conclusion, the study has shown an elevation of MPV and reduction of platelet count in acute stroke that persist long after the acute event[127].

MATERIALS AND METHODS

PATIENT SELECTION

The present study included diagnosed cases of type 2 diabetes patients on treatment from the department of diabetology, Government Stanley Medical College and Hospital, irrespective of their present glycemic status and the anti-glycemic agent being used for control of diabetes. Patients were then grouped into

INCLUSION CRITERIA

Confirmed cases of Type 2 DM, who are on treatment.

EXCLUSION CRITERIA

Cases of Type 1 DM.

Patients with abnormal platelet counts (thrombocytosis/thrombocytopenia)

Patients on anti-platelet medicines (aspirin, clopidogrel etc.).

History of blood dyscrasias

History of thyroid disorders.

Hb<8g%

PLACE OF STUDY

Stanley Medical College and Hospital, Chennai:

Department of General Medicine, Endocrinology OPD, Medical wards

SAMPLE SIZE: 100

STUDY DESIGN

Observational Study

ETHICAL COMMITTEE APPROVAL

Ethical committee approval was obtained for the study

HbA1C

HbA1C was estimated by immunoturbidometric method. The test principle Turbidimetric inhibition immunoassay (TINIA) for the in vitro determination of hemoglobinA1c in whole blood is as demonstrated in the following diagram.

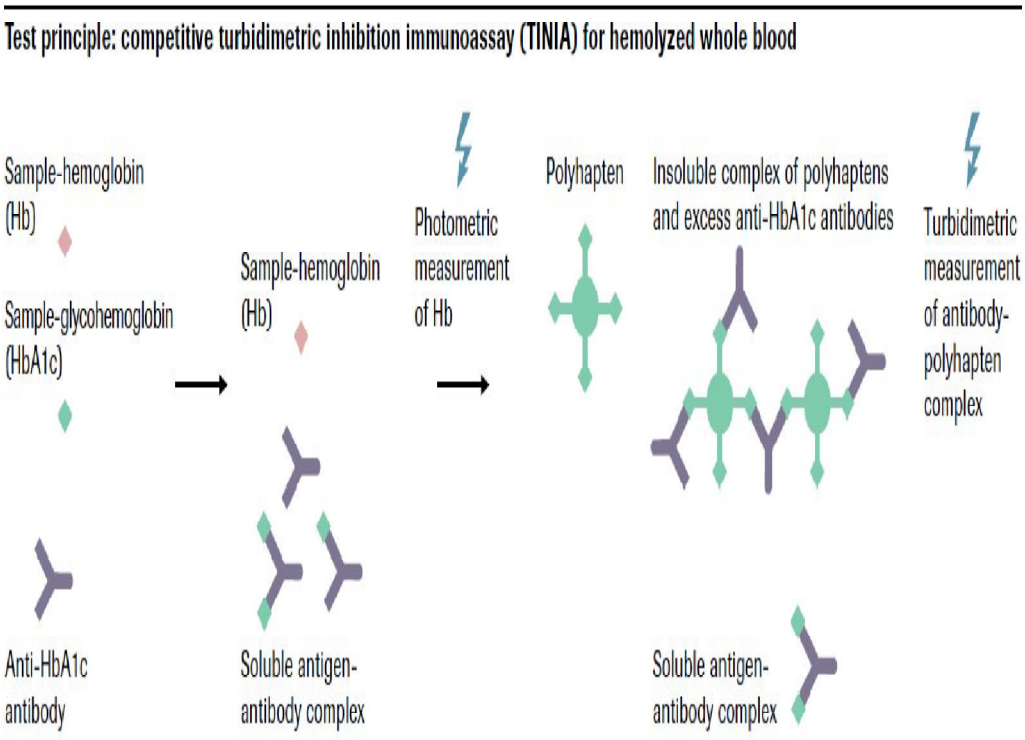


FIGURE 6: TEST PRINCIPLE FOR HbA1C USING COMPETITIVE TURBIDIMETRIC INHIBITION IMMUNOASSAY

PRINCIPLE BEHIND ESTIMATION OF MPV WITH SYSMEX SIX PART DIFFERENTIAL ANALYZER

The 6part differential sysmex analyzer is a fully automated bidirectional analyzer which performs hematological analysis according to the hemodynamic focusing, flow cytometry method (using semiconducted laser) and SLS-hemoglobin method.

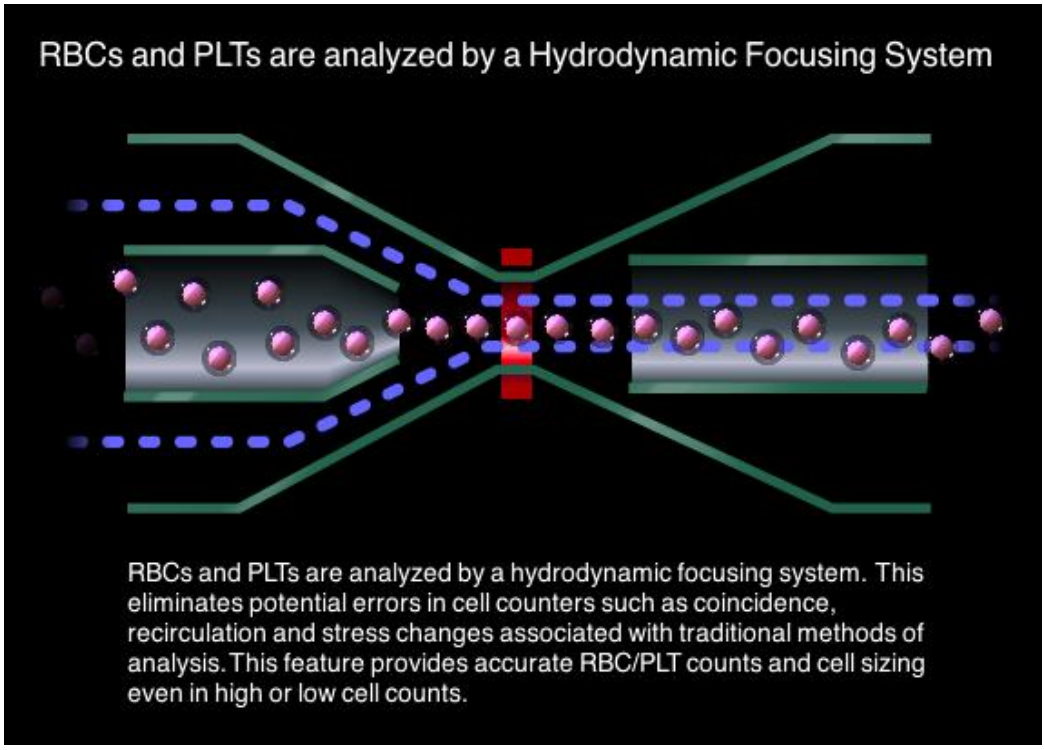


FIGURE 7: TEST PRINCIPLE BEHIND MPV ASSAY USING SYSMEX AUTO-ANALYSER

Serum cholesterol by CHOD PAP method and HDL and LDL by IFCC method in serum collected from plain venous sample.

STATISTICALANALYSIS

The collected data was analyzed with SPSS 16.0 version. To describe about the data descriptive statistics frequency analysis, percentage analysis were used for categorical variables and for continuous variables the mean and S.D were used. To find the significance difference between the bivariate samples in independent groups the Independent sample t-test was used. For the multivariate analysis the one way ANOVA was used. In both the above statistical tools the probability value .05 is considered as significant level.

RESULTS

The study was based on 100 diabetic patients who attended the medical and diabetology department of Government Stanley Medical College Hospital and who satisfied the inclusion as well exclusion criteria were enrolled for this study.

The collected data was analysed with SPSS 16.0 version.To describe about the data descriptive statistics frequency analysis, percentage analysis were used for categorical variables and for continuous variables the mean and S.D were used. To find the significance difference between the bivariate samples in independent groups the Independent sample t-test was used. For the multivariate analysis the one way ANOVA with Tukey's Post-Hoc test was used. In both the above statistical tools the probability value .05 is considered as significant level.

The detailed statistical analysis was done and the table showing the detailed descriptive statistics showing the mean, standad deviation, and range is given in the following page.

The data reveals the mean age of the subjects studied to be around 52 years, with amean HbA1C of 8.5 and mean MPV of 8.2.

TABLE 1: DESCRIPTIVE STATISTICS

Descriptive Statistics

	N	Range	Minimum	Maximum	Mean	Std. Deviation
Age	100	35	35	70	52.12	9.336
Height	100	.32	1.42	1.74	1.5888	.07400
Weight	100	42	42	84	62.34	8.336
BMI	100	14.03	18.20	32.23	24.7323	3.22809
Duration of Diabetes	100	22	1	22	4.45	3.606
SysBP	100	80	90	170	124.16	18.101
DysBP	100	30	60	90	76.50	7.322
Hb	100	5.1	9.2	14.3	11.258	1.0375
TC	100	9100	3800	12900	7377.21	1682.029
PLT	100	4.40	1.50	5.90	2.9943	.95744
MPV	100	5.6	5.2	10.8	8.246	1.0832
PDW	100	7	9	16	12.70	1.357
FBS	100	310	102	412	185.20	66.561
PPBS	100	441	121	562	232.18	81.249
HbA1C	100	9.5	5.6	15.1	8.575	1.8346
TCHOL	100	242	114	356	203.58	43.797
TGL	100	132	66	198	123.45	32.606
LDL	100	162	94	256	142.79	36.188
HDL	100	28	20	48	36.95	6.603
UREA	100	30	12	42	23.11	7.156
CREAT	100	1.1	.1	1.2	.484	.3064
T3	100	137	62	199	131.02	39.042
T4	100	6.9	4.3	11.2	7.800	1.9732
TSH	100	5.3	.3	5.6	2.718	1.4620
Valid N (listwise)	100					

Among the 100 patients 58 were female and 42 were males, with an average age of 52.12 (SD 9.336), the youngest among the lot being 35 yrs and the eldest being 70 yrs.

TABLE 2: DETAILS OF AGE

	N	Range	Minimum	Maximum	Mean	Std. Deviation
Age	100	35	35	70	52.12	9.336

In studied group,majority of cases were from the age group of 41-50 years.

TABLE 3:DETAILS OF AGE RANGE

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Upto 40 yrs	14	14.0	14.0	14.0
	41 to 50 yrs	34	34.0	34.0	48.0
	51 to 60 yrs	28	28.0	28.0	76.0
	Above 60 yrs	24	24.0	24.0	100.0
	Total	100	100.0	100.0	

FIGURE1:AGE DISTRIBUTION RANGE

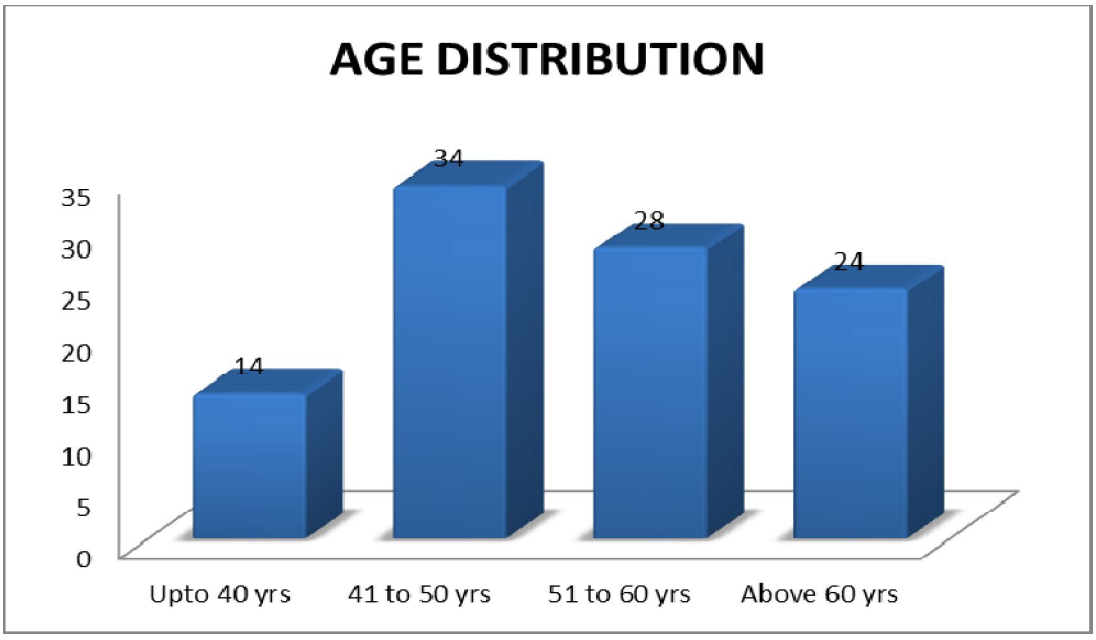


FIGURE 2: GENDER DISTRIBUTION

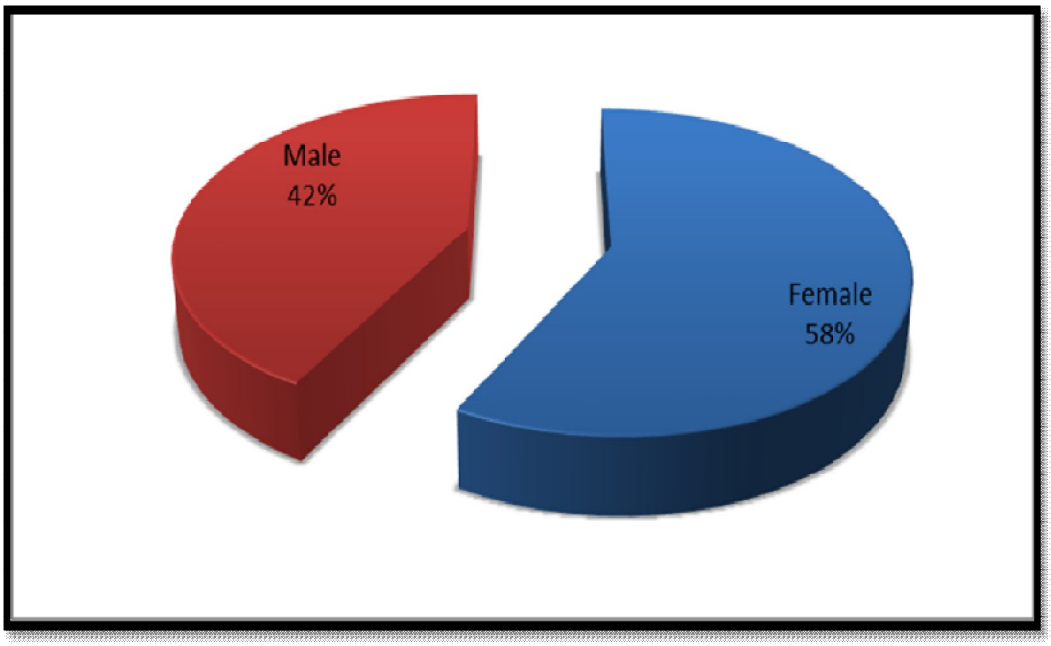


TABLE 4: GENDERWISE DISTRIBUTION OF PATIENTS IN THE STUDY

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Female	58	58.0	58.0	58.0
	Male	42	42.0	42.0	100.0
	Total	100	100.0	100.0	

Out of 100 patients, 58 were females whereas ,42 were male. Thus majority of patients were females.

TABLE 5:TREATMENT PROFILE

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	D	1	1.0	1.0	1.0
	O	90	90.0	90.0	91.0
	O+I	9	9.0	9.0	100.0
	Total	100	100.0	100.0	

Of the 100 patients studied, the majority were on oral hypoglycaemic agents alone(O), a few on both insulin and oral hypoglycaemics (O+I), and one person on diet management.

FIGURE 3: TREATMENT PROFILE

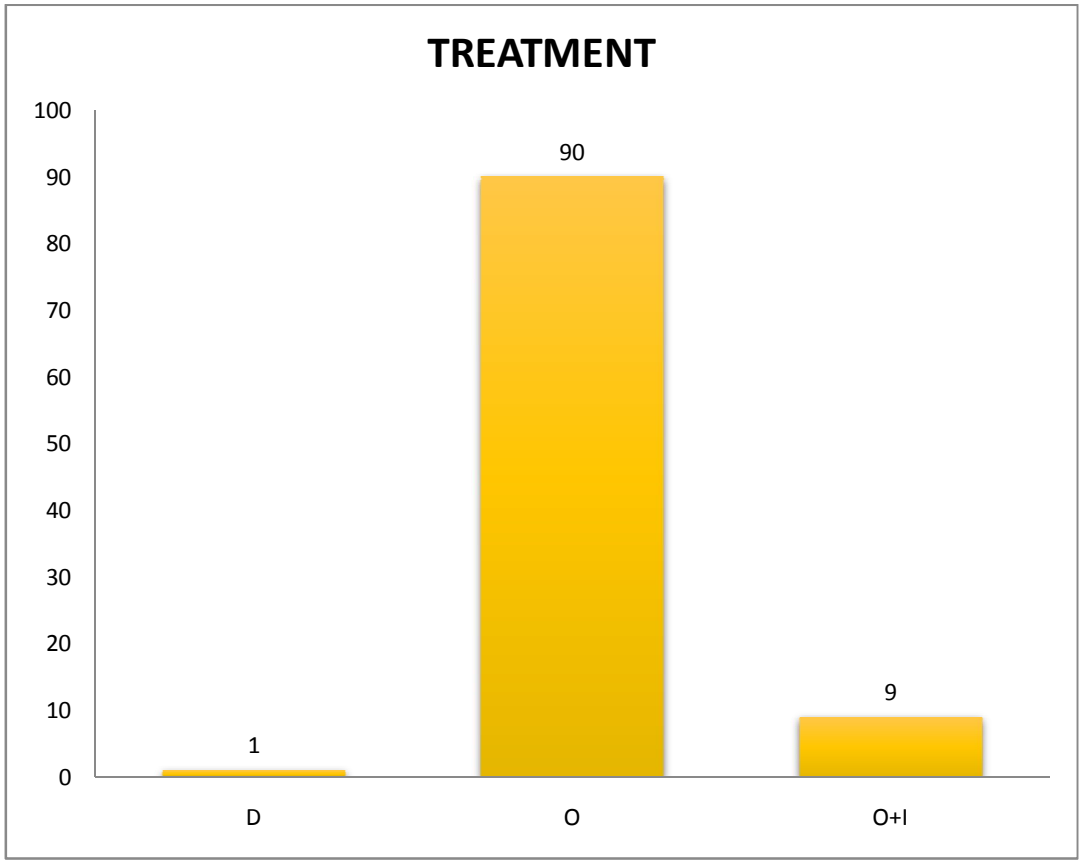


TABLE 6 :HISTORY OF ALCOHOL

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	NO	72	72.0	72.0	72.0
	YES	28	28.0	28.0	100.0
	Total	100	100.0	100.0	

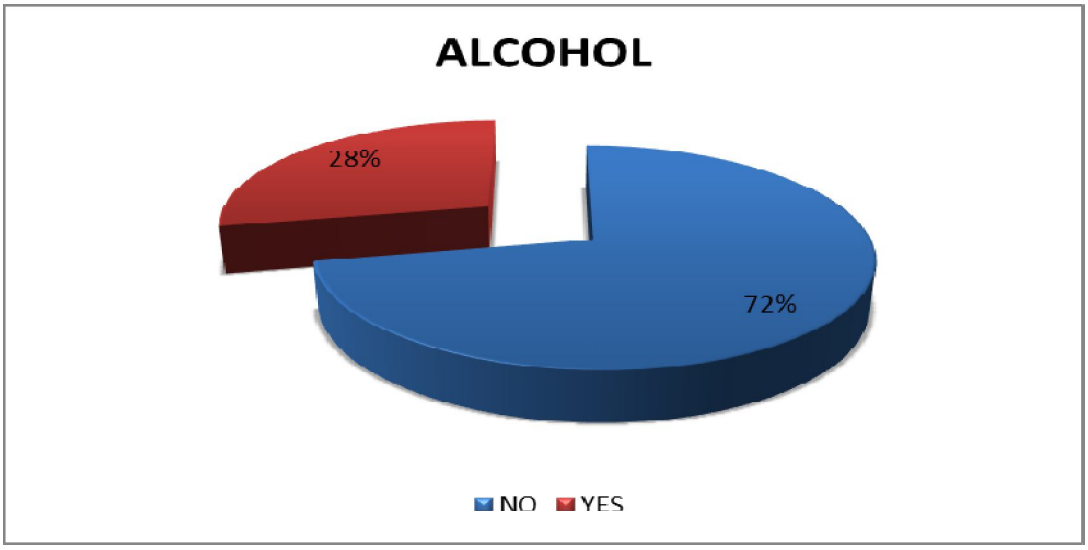


FIGURE 4: ALCOHOL EXPOSURE

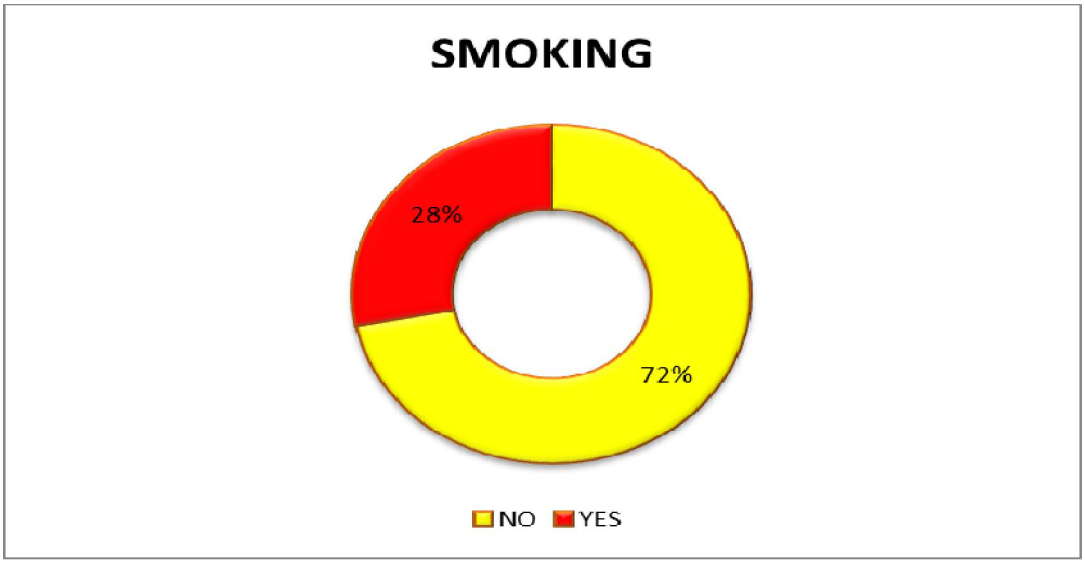


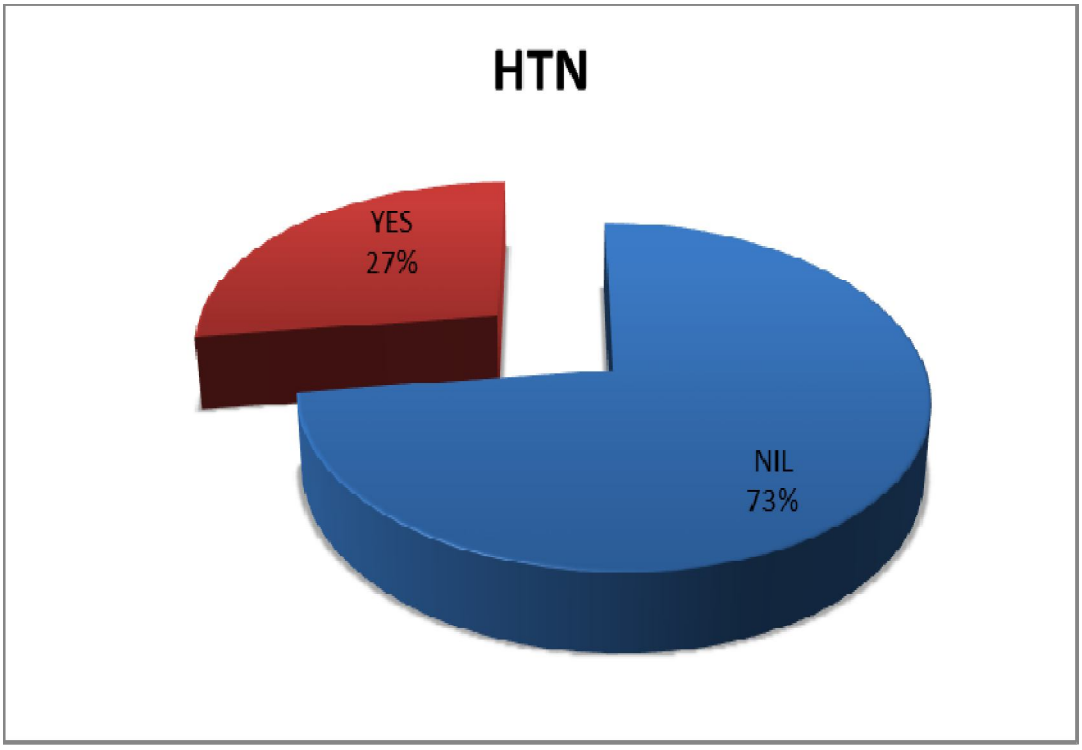
FIGURE 5: SMOKING HISTORY

In the population studied around 74 people had either alcohol or smoking exposure, of which 70 subjects gave history of both alcoholism and smoking.

TABLE 7 : HYPERTENSION HISTORY

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	NIL	73	73.0	73.0	73.0
	YES	27	27.0	27.0	100.0
	Total	100	100.0	100.0	

FIGURE 6 :HYPERTENSION HISTORY



In the population studied, 27% gave a history of hypertension on treatment with controlled blood pressure values.

TABLE 8 : WEIGHT WISE DISTRIBUTION OF PATIENTS IN STUDY

Weightrange

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Below 50 kgs	6	6.0	6.0	6.0
	50 to 70 kgs	78	78.0	78.0	84.0
	Above 70 kgs	16	16.0	16.0	100.0
	Total	100	100.0	100.0	

TABLE 9 :BMI RANGE OF PATIENTS IN STUDY

BMIrange

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	18 to 24	43	43.0	43.0	43.0
	24.1 to 30	47	47.0	47.0	90.0
	Above 30	10	10.0	10.0	100.0
	Total	100	100.0	100.0	

In the population studied the BMI range of the patients were mainly in the range of 24.1-30. Ten percentage were in the range of BMI above 30.

FIGURE 7 :WEIGHT RANGE

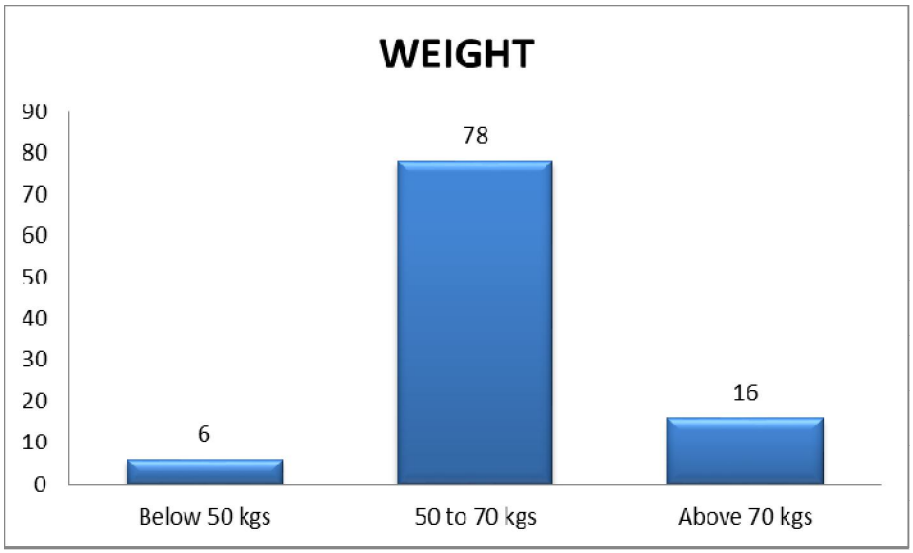
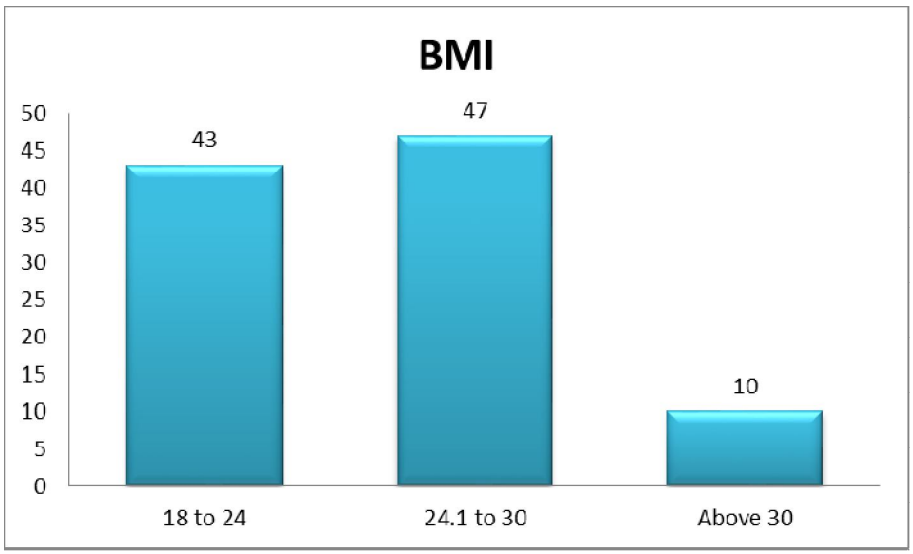


FIGURE 8 : BMI RANGE



The cholestrol levels in the population was as plotted below in the table and figure,with a minimal 22% subjects with undesirable level of cholesterol. And among the hundred subjects studied 17 subjects had abnormal levels of triglycerides.

TABLE 10 : CHOLESTEROL LEVELS IN THE STUDY POPULATION

Cholesterol

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Desirable	60	60.0	60.0	60.0
	Border line	18	18.0	18.0	78.0
	Undesirable	22	22.0	22.0	100.0
	Total	100	100.0	100.0	

TABLE 11 : TGL LEVELS IN THE STUDY POPULTION

TGLrange

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Normal	83	83.0	83.0	83.0
	Abnormal	17	17.0	17.0	100.0
	Total	100	100.0	100.0	

The following tables gives the details of the HDL and LDL levels of the subjects in the population studied which shows a low and undesirable level of HDL in 17% and 28% showed an elevated levels of LDL .

TABLE 12:HDL LEVELS IN STUDY POPULATION

HDLrange

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Undesirable	17	17.0	17.0	17.0
	Border line	83	83.0	83.0	100.0
	Total	100	100.0	100.0	

TABLE 13 :LDL LEVELS IN STUDY POPULATION

LDLrange

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Normal	42	42.0	42.0	42.0
	Low risk	30	30.0	30.0	72.0
	High risk	28	28.0	28.0	100.0
	Total	100	100.0	100.0	

FIGURE 9 :CHOLESTEROL LEVELS IN THE STUDY POPULATION

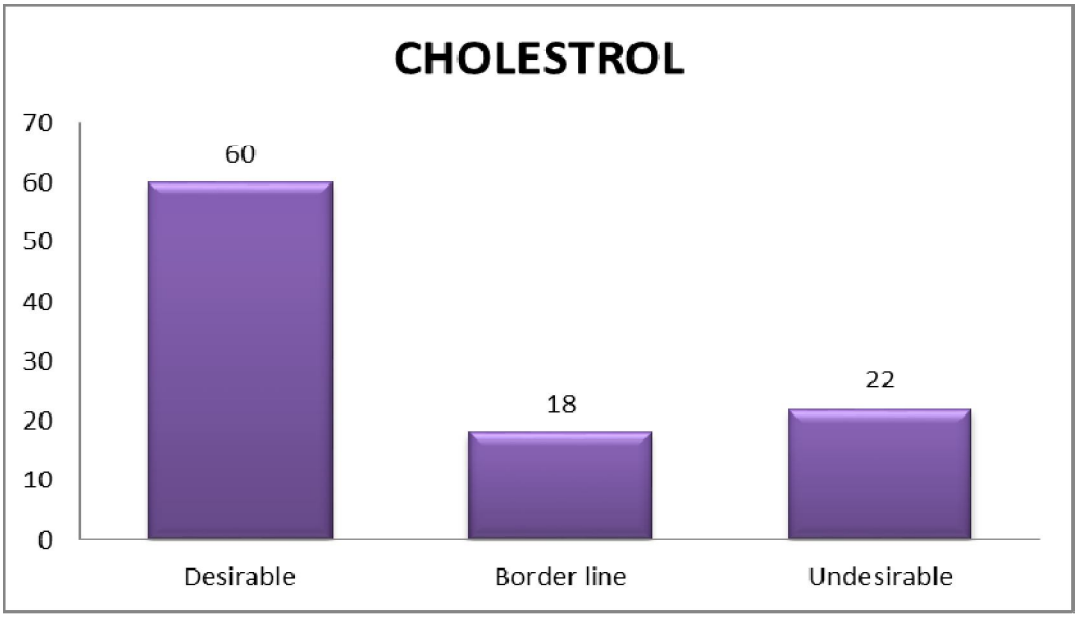


FIGURE 10 :TGL LEVELS IN THE STUDY POPULATION

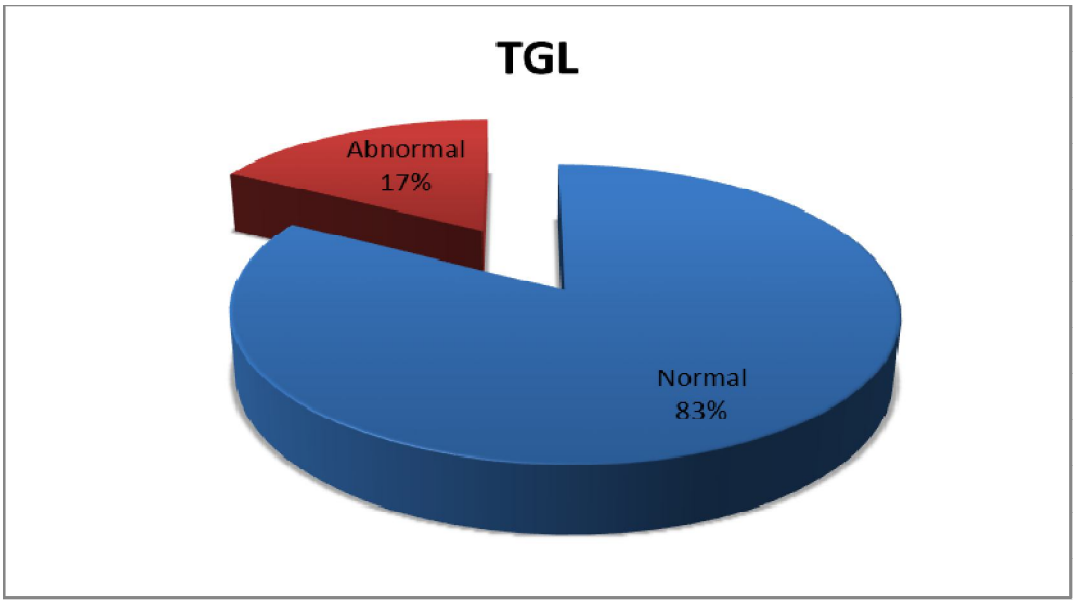


FIGURE 11 :HDL LEVELS IN THE STUDY POPULATION

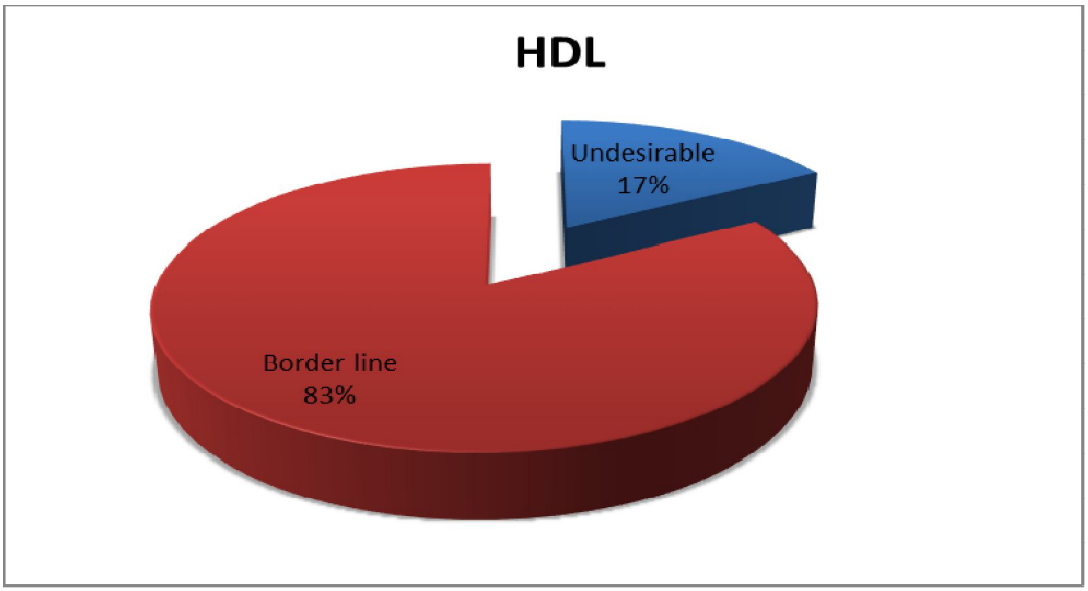
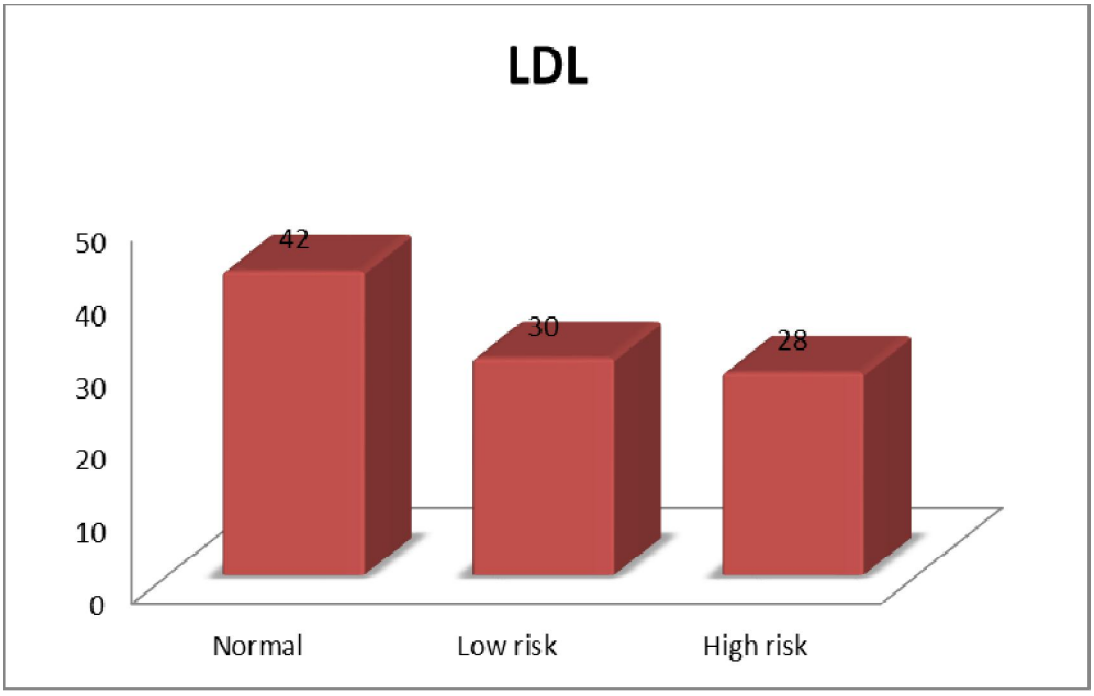


FIGURE12 :LDL LEVELS IN THE STUDY POPULATION



The FBS and PPBS range of the diabetic subjects of the study showed 71% with poor control of FBS and 44% with elevated PPBS values.

TABLE 14 : FBS LEVELS IN STUDY POPULATION

FBSrange

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Good Control	29	29.0	29.0	29.0
	Poor Control	71	71.0	71.0	100.0
	Total	100	100.0	100.0	

TABLE 15 : PPBS LEVELS IN STUDY POPULATION

PPBSrange

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	> 200	44	44.0	44.0	44.0
	< 200	56	56.0	56.0	100.0
	Total	100	100.0	100.0	

FIGURE13 : FBS LEVELS IN THE STUDY POPULATION

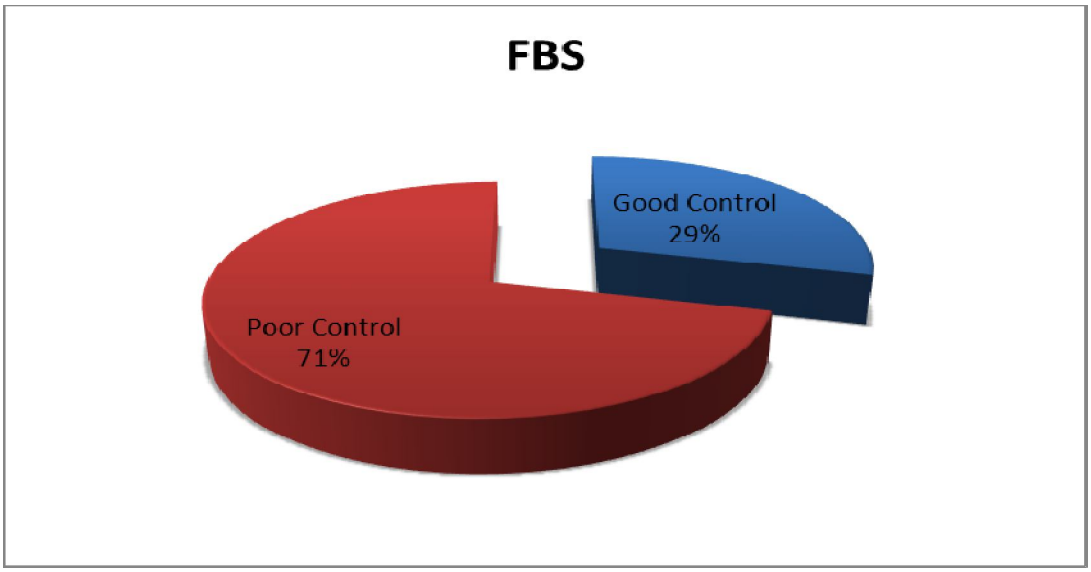
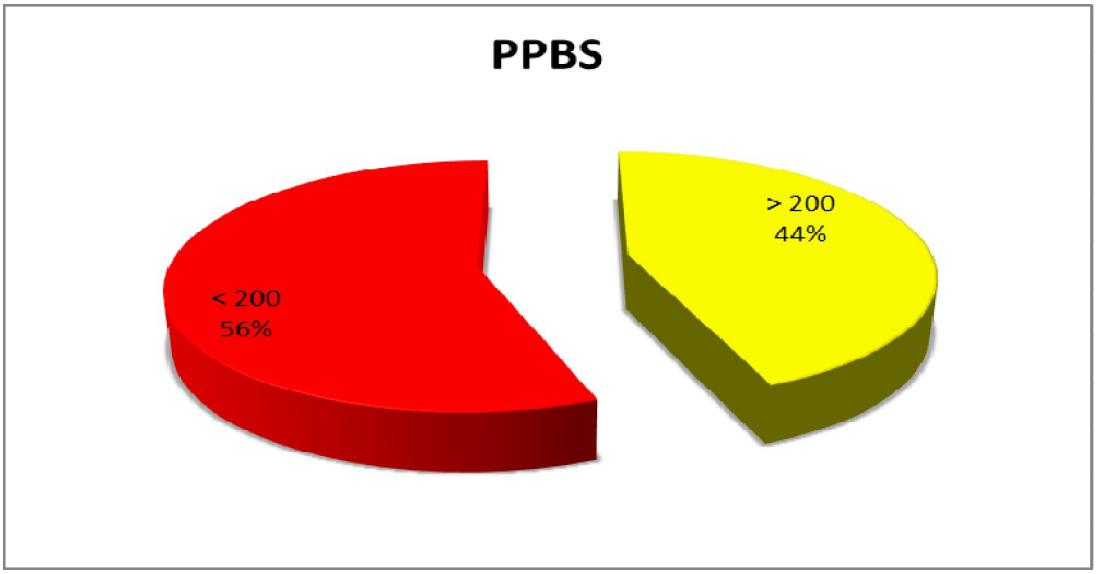


FIGURE14 : PPBS LEVELS IN THE STUDY POPULATION



In the population studied 53% of the subjects had an HbA1C of more than 8 and 18% showed a good control of HbA1C of less than 7.

TABLE 16 : HbA1C RANGE IN STUDY POPULATION

HbA1Crange

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Good Control	18	18.0	18.0	18.0
	Fair Control	29	29.0	29.0	47.0
	Poor Control	53	53.0	53.0	100.0
	Total	100	100.0	100.0	

FIGURE 15 :HbA1C RANGE IN STUDY POPULATION

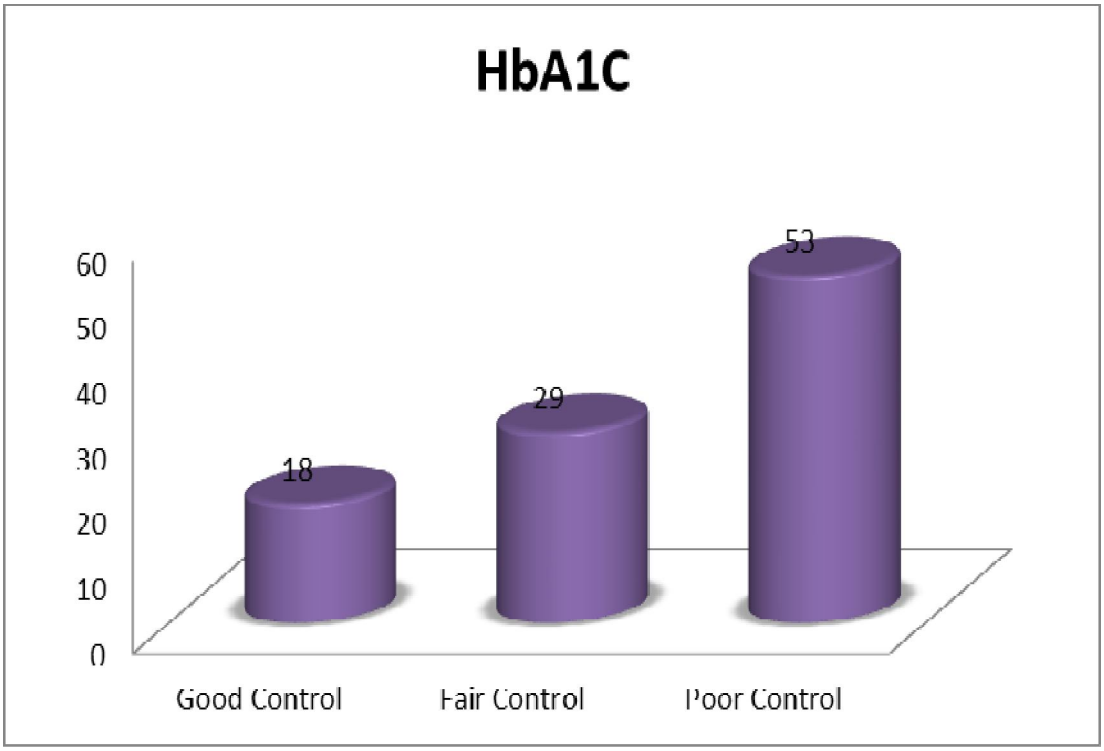


TABLE 17 :MPV RANGE IN STUDY POPULATION

MPVrange

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	< 9	77	77.0	77.0	77.0
	> 9	23	23.0	23.0	100.0
	Total	100	100.0	100.0	

In the population studied the MPV in 77% of the subjects were below 9fl and the rest of the 23% showed MPV more than 9 fl.

TABLE 18 :COMPARISON OF MPV WITH FBS VALUES

	FBSrange	N	Mean	Std. Deviation	Std. Error Mean
MPV	Good Control	29	8.028	.8623	.1601
	Poor Control	71	8.335	1.1551	.1371

The MPV in the study population was compared with the FBS values, with T-test which demonstrated a relation which was not statistically significant(p=.199) .

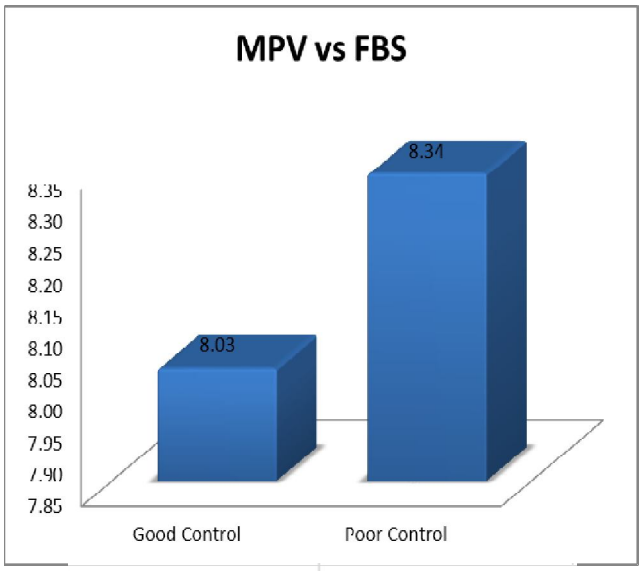
TABLE19 :COMPARISON OF MPVWITH FBS VALUES

STATISTICS

	t value	Pvalue	Mean Difference	Std. Error Difference
MPV	-1.293	.199	-.3076	.2379
	-1.459	.149	-.3076	.2108

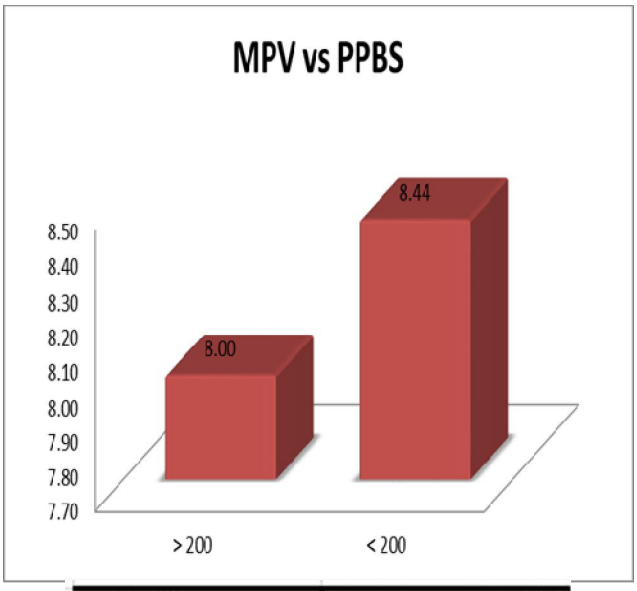
FIGURE 17 : COMPARISON OF MPV IN PATIENTS WITH

GOOD CONTROL VS POOR CONTROL OF FBS



	MPV vs FBS
Good Control	8.03
Poor Control	8.34

FIGURE 18 : COMPARISON OFMPV AND PPBS



> 200	8.00
< 200	8.44

TABLE 19: COMPARISON OFMPV AND PPBS

Group Statistics

	PPBSrange	N	Mean	Std. Deviation	Std. Error Mean
MPV	> 200	44	7.998	.9648	.1455
	< 200	56	8.441	1.1385	.1521

The MPV in the study population was compared with the PPBS values, with T-test which demonstrated a relation which was statistically significant(p=.042) .

TABLE 20:COMPARISON OF MPV AND PPBS, STATISTICS

	t	P value	Mean Difference	Std. Error Difference
MPV	-2.065	.042	-.4433	.2147
	-2.106	.038	-.4433	.2105

TABLE 21 :COMPARISON OF MPV AND TGL

Group Statistics

	TGLrange	N	Mean	Std. Deviation	Std. Error Mean
MPV	Normal	83	8.263	1.1110	.1219
	Abnormal	17	8.165	.9624	.2334

The MPV in the study population was compared with the TGL values, with T-test which demonstrated a relation which was not statistically significant(p=.736) .

TABLE 22 : COMPARIS)ON MPV AND TGL STATISTICS

	t	P value	Mean Difference	Std. Error Difference
MPV	.338	.736	.0979	.2897
	.372	.713	.0979	.2633

TABLE 23:COMPARISON OF MPV AND HDL

Group Statistics

	HDLrange	N	Mean	Std. Deviation	Std. Error Mean
MPV	Undesirable	17	8.171	.9700	.2353
	Border line	83	8.261	1.1098	.1218

The MPV in the study population was compared with the HDL values, with T-test which demonstrated a relation which was not statistically significant(p=.754) .

TABLE 24:COMPARISON OFMPV AND HDL STATISTICS

	T test	P value	Mean Difference	Std. Error Difference
MPV	-.314	.754	-.0909	.2897
	-.343	.734	-.0909	.2649

FIGURE 19 : COMPARISON OF MPV AND HDL

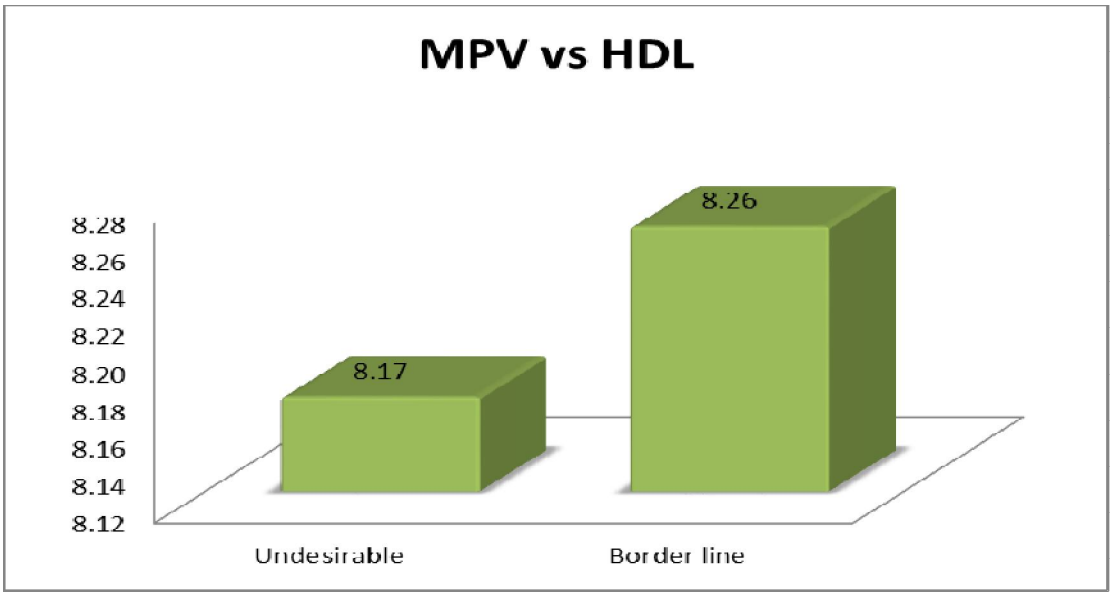
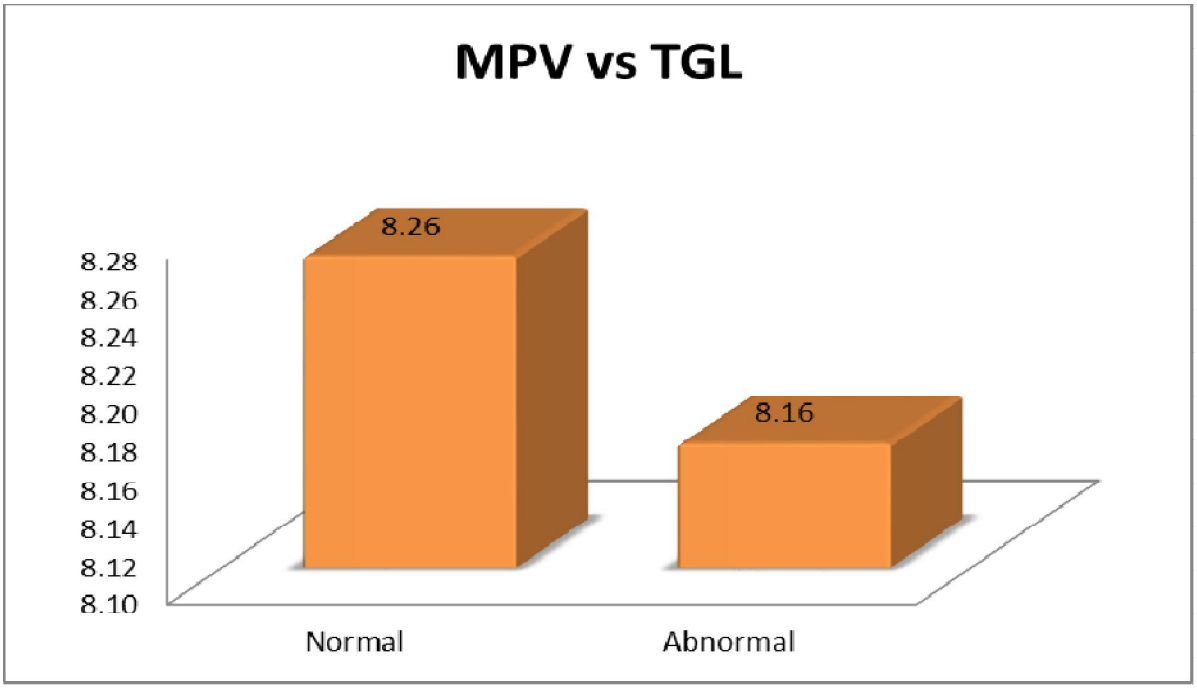


FIGURE 20 : COMPARISON OF MPV AND TGL



Group Statistics

	Sex	N	Mean	Std. Deviation	Std. Error Mean
MPV	Female	58	8.403	1.1198	.1470
	Male	42	8.029	1.0032	.1548

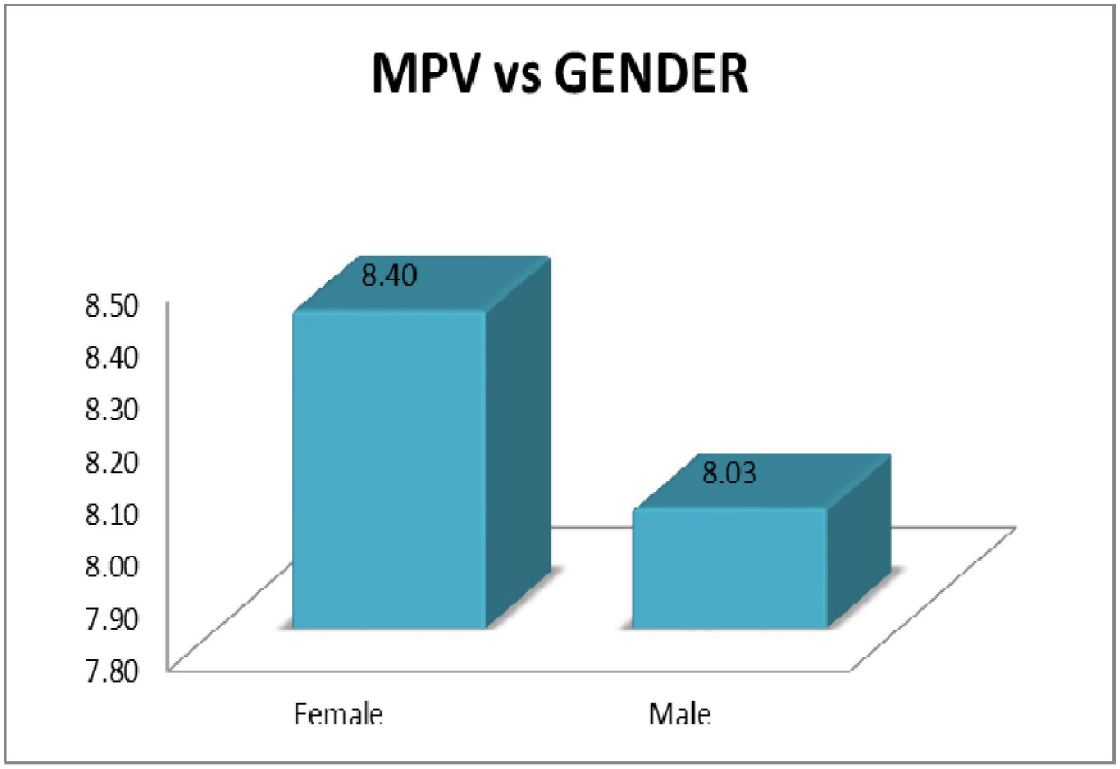
TABLE 25 : COMPARISON OF MPV AND GENDER

		T value	P value	Mean Difference	Std. Error Difference
MPV	F	1.725	.088	.3749	.2173
	M	1.756	.082	.3749	.2135

TABLE 26 : COMPARISON OF MPV AND GENDER STATISTICS

FIGURE21:COMPARISON OF MPV AND GENDER

Female	8.40
Male	8.03



The MPV in the study population was compared with gender, which showe a higher value of MPV in females compared to the male population. But this was not statistically significant(p=.088), when analysed by the T-test .

TABLE 27 : COMPARISON OF MPV AND HbA1C

	N	Mean	Std. Deviation	Std. Error
Good Control	18	7.289	.7866	.1854
Fair Control	29	7.897	.6593	.1224
Poor Control	53	8.762	1.0681	.1467
Total	100	8.246	1.0832	.1083

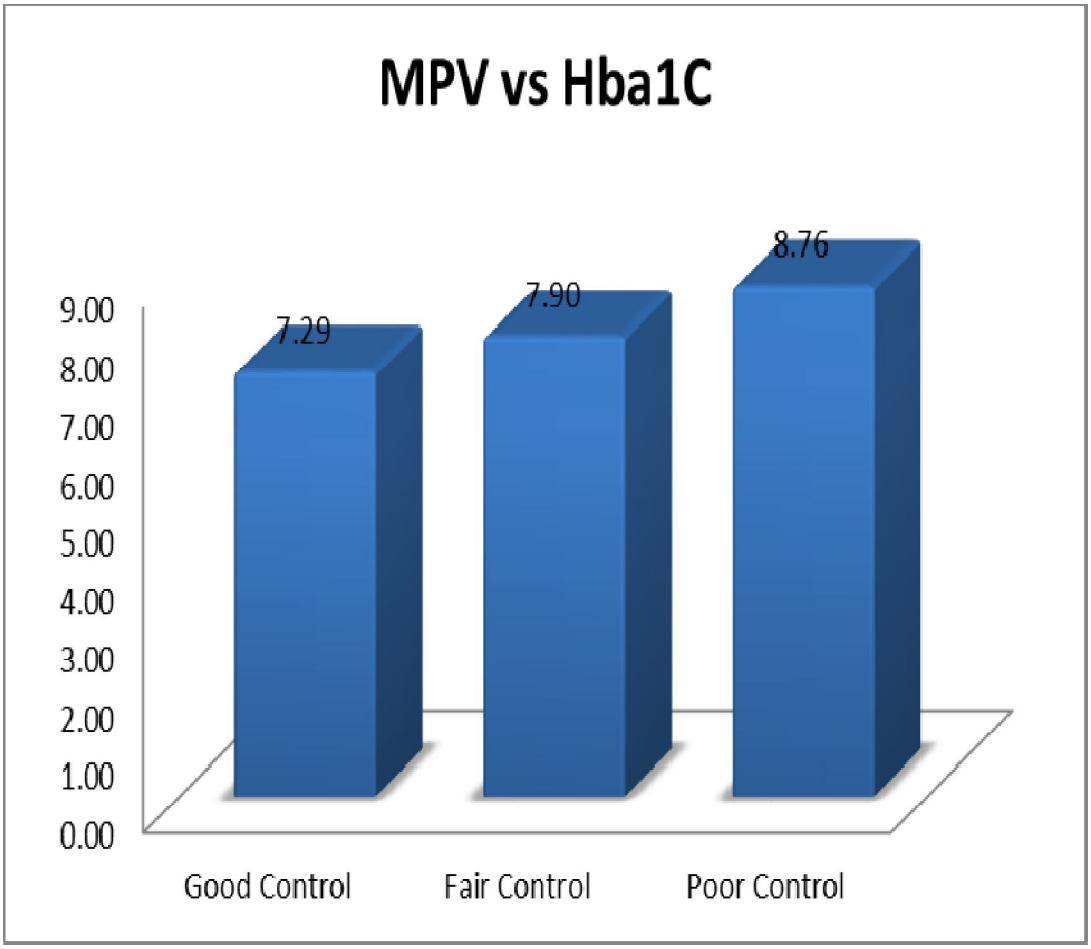
The descriptive statistics showing the relation between mean platelet volume and HbA1C is shown in the above table with a mean of 8.246 in the total subjects studied and 8,762 in the subjects with poor control (HbA1C > 8%) and 7.289 in the subjects with good glycemic control.

TABLE 29 : COMPARISON OF MPV AND HbA1C

STATISTICS

(I) HbA1Crange		Mean Difference (I-J)	Std. Error	Sig.
Good Control	Fair Control	-.6077	.2759	.076
	Poor Control	-1.4734	.2508	0.0001
Fair Control	Good Control	.6077	.2759	.076
	Poor Control	-.8657	.2124	0.0001
Poor Control	Good Control	1.4734	.2508	0.0001
	Fair Control	.8657	.2124	0.0001

FIGURE 22: COMPARISON OF MPV AND HbA1C



The MPV in the study population was compared with the HbA1C values, with ANOVA demonstrated a relation which was statistically significant(p=.000) .

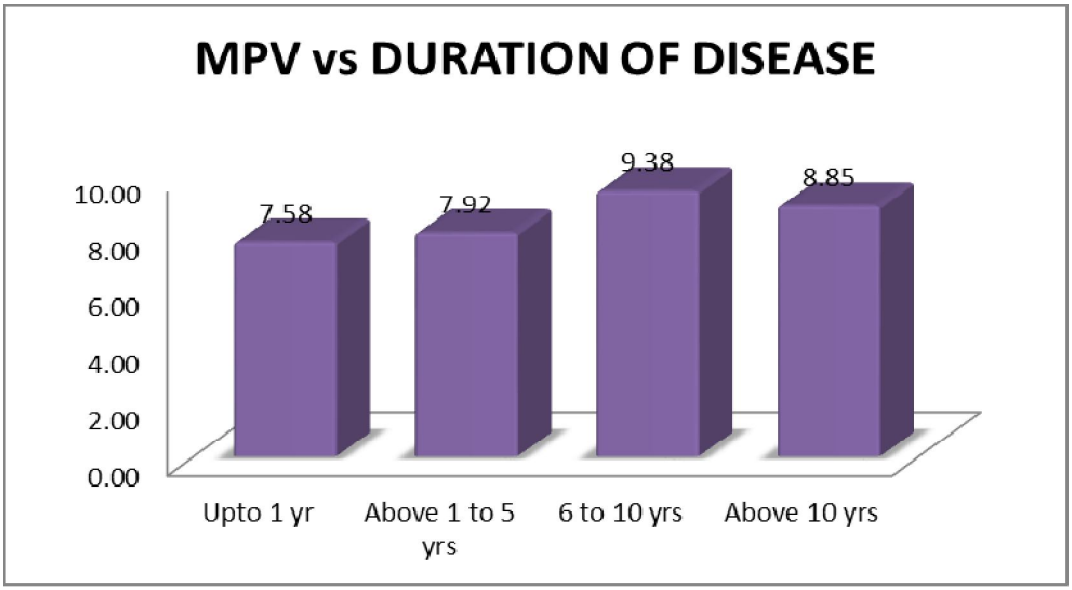
TABLE 30:COMPARISON OF MPV AND DURATION OF DIABETES

	N	Mean	Std. Deviation	Std. Error
Upto 1 yr	19	7.584	.9963	.2286
Above 1 to 5 yrs	52	7.915	.8619	.1195
6 to 10 yrs	23	9.383	.7346	.1532
Above 10 yrs	6	8.850	.7259	.2964
Total	100	8.246	1.0832	.1083

TABLE 31:COMPARISON OF MPV AND DURATION OF DIABETES STATISTICS

(I) Duration		Mean Difference (I-J)	Std. Error	Sig.
Upto 1 yr	Above 1 to 5 yrs	-.3312	.2293	.475
	6 to 10 yrs	-1.7984	.2652	.000
	Above 10 yrs	-1.2658	.4006	.011
Above 1 to 5 yrs	Upto 1 yr	.3312	.2293	.475
	6 to 10 yrs	-1.4672	.2142	.000
	Above 10 yrs	-.9346	.3689	.061
6 to 10 yrs	Upto 1 yr	1.7984	.2652	.000
	Above 1 to 5 yrs	1.4672	.2142	.000
	Above 10 yrs	.5326	.3922	.529
Above 10 yrs	Upto 1 yr	1.2658	.4006	.011
	Above 1 to 5 yrs	.9346	.3689	.061
	6 to 10 yrs	-.5326	.3922	.529

FIGURE 23 :COMPARISON OF MPV AND DURATION OF DIABETES



Upto 1 yr	7.58
Above 1 to 5 yrs	7.92
6 to 10 yrs	9.38
Above 10 yrs	8.85

The MPV in the study population was compared with the duration of diabetes, with ANOVA demonstrated a relation which was statistically significant(p=.011) .

TABLE 32:COMPARISON OF MPV AND DURATION OF DIABETES STATISTICS

DURATION	N	MPV
Upto 1 yr	19	7.584
Above 1 to 5 yrs	52	7.915
Above 10 yrs	6	8.850
6 to 10 yrs	23	9.383

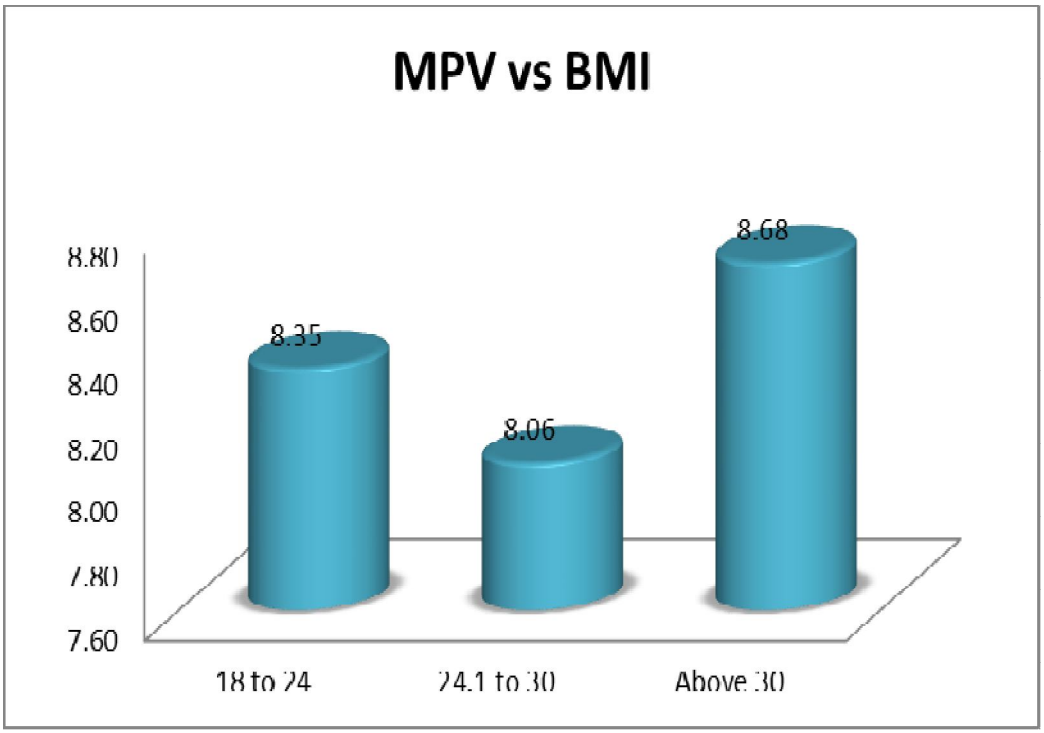
The variation in MPV values in the study population with regard to the duration of diabetes was studied, although the age group size are unequal.

TABLE 33:COMPARISON OF MPV AND BMI DESCRIPTIVE STATISTICS

	N	Mean	Std. Deviation	Std. Error
18 to 24	43	8.351	.9804	.1495
24.1 to 30	47	8.057	1.1517	.1680
Above 30	10	8.680	1.0932	.3457
Total	100	8.246	1.0832	.1083

In the study population MPV in various BMI ranges were analysed but the relation was not statistically sinificant with a p value of 0.180.

FIGURE 24:COMPARISON OF MPV AND BMI



	MPV vs BMI
18 to 24	8.35
24.1 to 30	8.06
Above 30	8.68

The MPV in the study population was compared with the BMI, with ANOVA demonstrated a relation which was not statistically significant(p=.180) .

TABLE 34: COMPARISON OF MPV AND AGE

	N	Mean	Std. Deviation	Std. Error
Upto 40 yrs	14	7.614	.5921	.1582
41 to 50 yrs	34	8.056	1.0299	.1766
51 to 60 yrs	28	8.264	1.1716	.2214
Above 60 yrs	24	8.863	1.0129	.2068
Total	100	8.246	1.0832	.1083

The descriptive statistics of the study population showing the mean platelet volume in different age groups in the study population.

(I) Agerange (J) Agerange	Mean Difference (IJ)	Std. Error	Sig.
Upto 40 yrs 41 to 50 yrs	-.4416	.3245	.527
51 to 60 yrs	-.6500	.3344	.217
Above 60 yrs	-1.2482	.3436	003
41 to 50 yrs Upto 40 yrs	.4416	.3245	.527
51 to 60 yrs	-.2084	.2607	.855
Above 60 yrs	-.8066	.2724	.020
51 to 60 yrs Upto 40 yrs	.6500	.3344	.217
41 to 50 yrs	.2084	.2607	.855
Above 60 yrs	-.5982	.2842	.159
Above 60 yrs Upto 40 yrs	1.2482	.3436	.003
41 to 50 yrs	.8066	.2724	.020
51 to 60 yrs	.5982	.2842	.159

TABLE 37 : COMPARISON OF MPV AND AGE

FIGURE25: COMPARISON OF MPV AND AGE

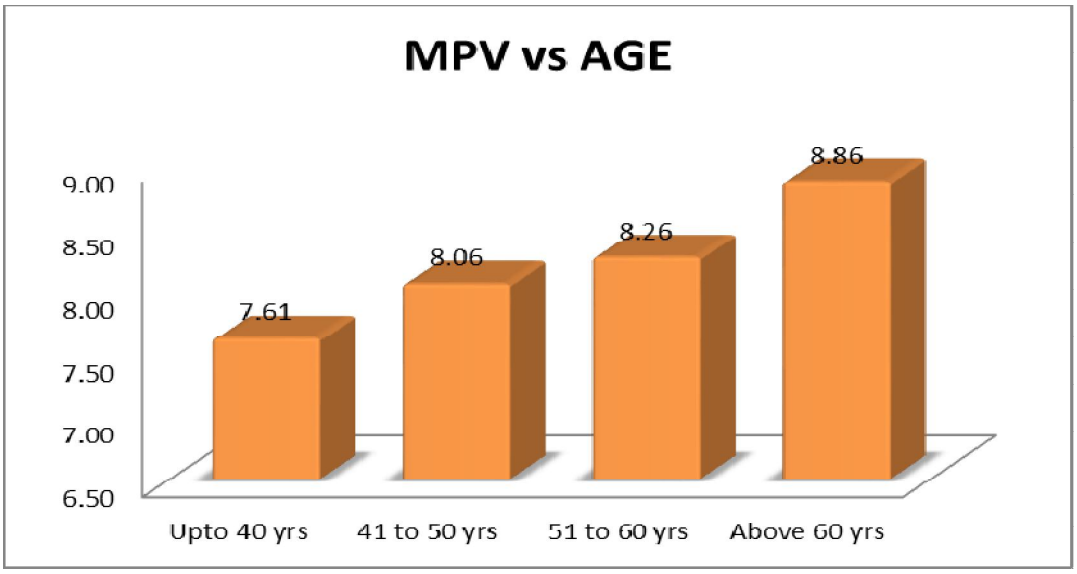


TABLE 38 : COMPARISON OF MPV AND AGE

AGE RANGE	N	MPV
UPTO 40 YRS	14	7.164
41-50 YRS	34	8.056
51-60YRS	28	8.264
ABOVE 60YRS	24	8.863

	MPV
Duration of Diabetes t value	0.521
P value	0.0001
N	100

TABLE 39 : CORRELATION OF MPV AND DURATION OF DIABETES

In conclusion, in the study the duration of diabetes was significantly related to the MPV is significant at 0.01 level.Also the HbA1C was significantly related to the MPV at 0.01 level of significance.

TABLE 40:CORRELATION OF MPV AND HbA1C

		MPV
HbA1C	t value	0.676
	P value	0.0001
	N	100

A highly significant correlation was noted between HbA1C and MPV with a T value of 0.676 and p value of 0.0001 among the hundred patients studied.

TABLE41:CORRELATION OF MPV AND DURATION OF DIABETES AND HbA1C

VARIABLE	t value	P value	Inference
Duration of diabetes	0.521	0.0001	Highly significant
HbA1C	0.676	0.0001	Highly significant

Finally charting the study in a table, showing the significant relation of MPV and durationof diabetes and HbA1C at significance level of 0.0001.

In the above table, the result of the study is charted as the correlation between the mean platelet volume and duration of diabetes with a t value of 0.521 and p value of 0.0001 which is highly significant. Also, the relationof glycated hemoglobin and mean platelet volume showed a t value 0f 0.676 and a highly significant p value of 0.00001.

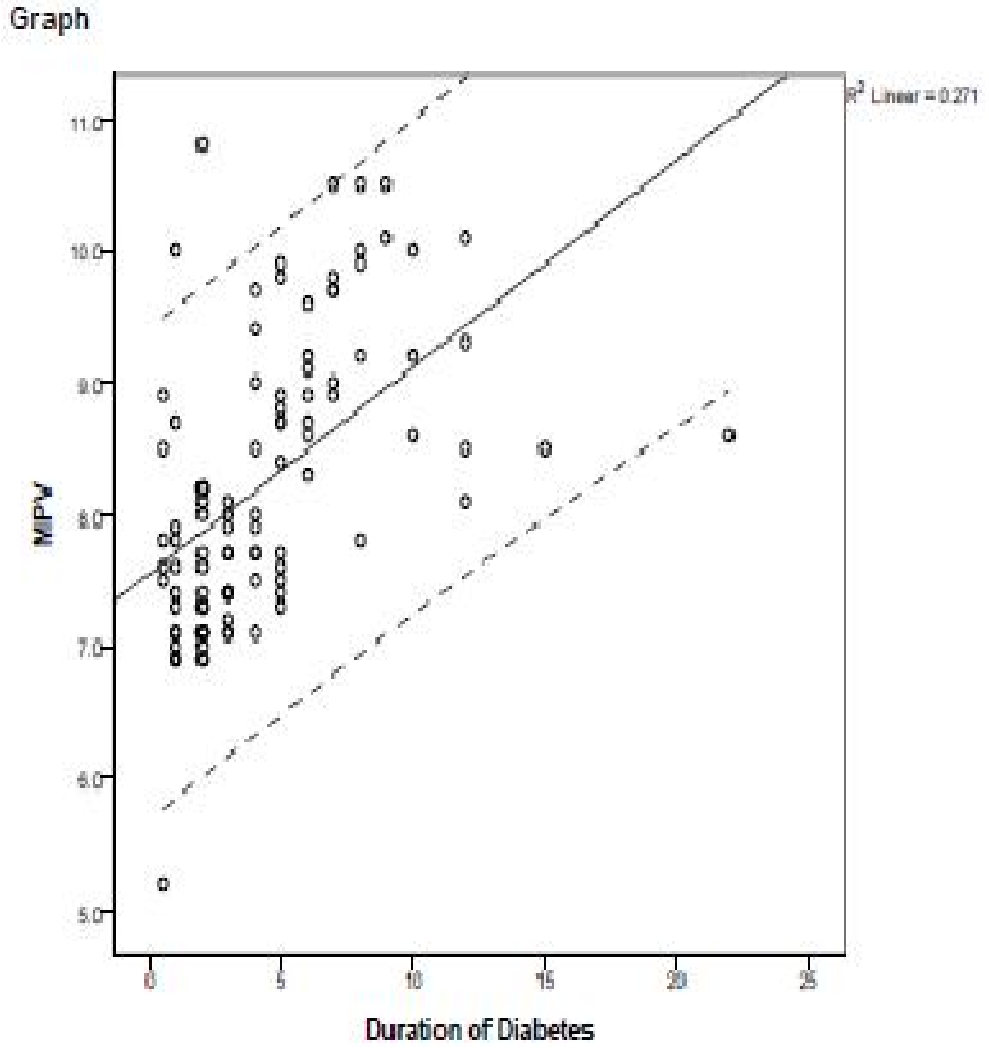


FIGURE 26: GRAPHICAL REPRESENTATION OF MPV DISTRIBUTION WITH DURATION OF DIABETES

A linear relation with MPV and duration of diabetes was noted in the study.

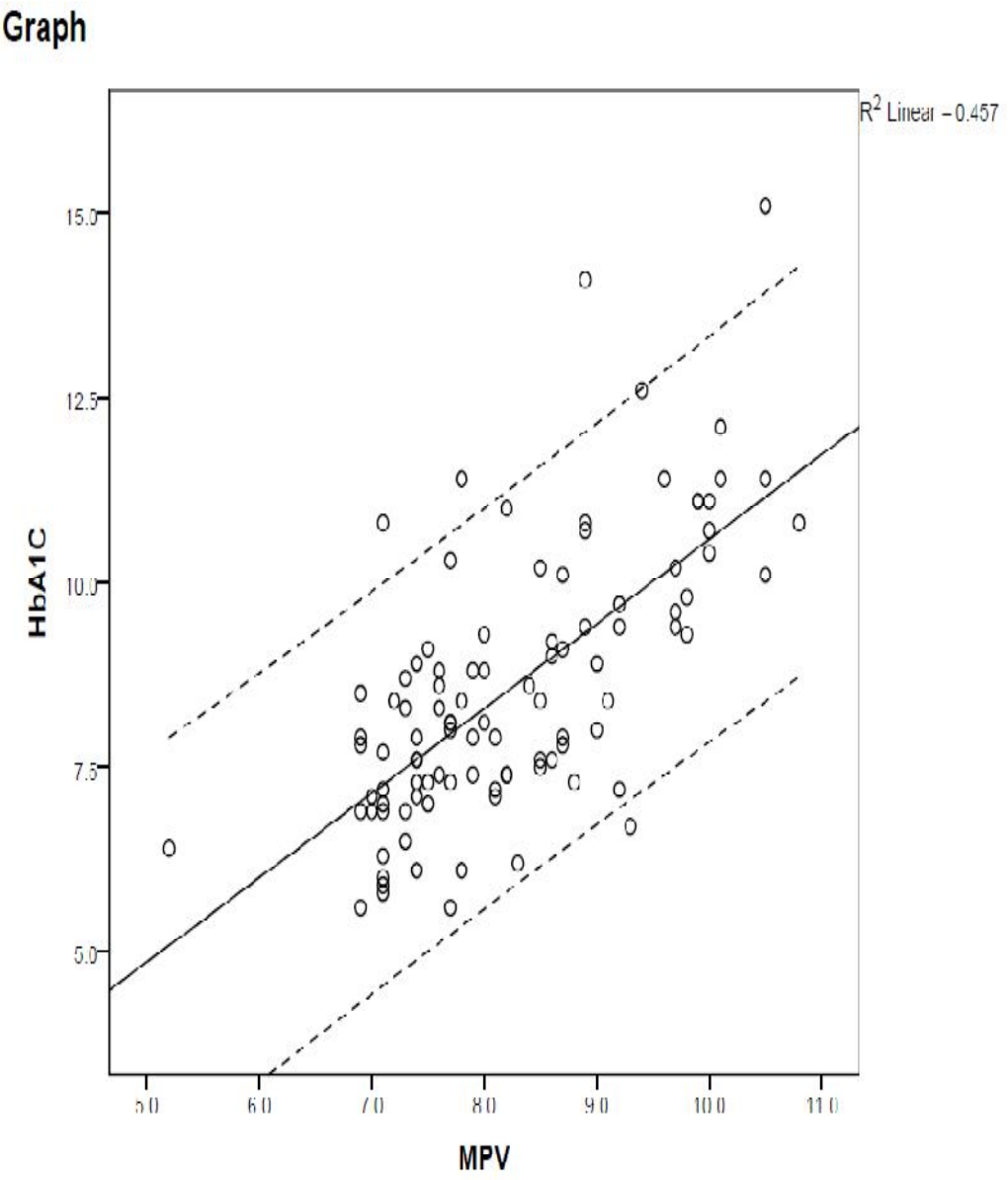


FIGURE 26: GRAPHICAL REPRESENTATION OF MPV DISTRIBUTION WITH HbA1C

A linear relation was noted with MPV with increasing HbA1C values.

DISCUSSION

This study conducted at Government Stanley Hospital with an aim to identify the effect of glycemic control on mean platelet volume. This is cross sectional study aimed at population consulting at medical departments and the department of diabetology of Government Stanley Hospital.

Following passages will describe and discuss the study finding in comparison with standard data and reviews available for mean platelet volume and its relation to glycemic control.

Previous studies have documented various platelet abnormalities especially an increase in mean platelet volume in diabetic subjects.

The average age of patients enrolled in the study was 52.12 years. In the subjects studied majority were in the age group of 41-50 years of age, with 34%, and then the age group of 51-60 years with 28% and 24% in the age group of above 60 years. 14% of the subjects were below 40 years of age.

Out of the 100 patients studied 58 were females and 48 males, thus a majority of female subjects were included in this study(58%).

In the study by Shah B et al. published in 2012 studied 13021 subjects of which 1558 were diabetic patients. In the study 48% were males with the predominance of females by 52%, similar to the current study. The mean age of the population studied was 47 years with subjects of age ranging from 21 to 85 years of age. In the study the population was divided into 3 groups according to their HbA1C levels and it was found that the mean platelet volume in patients with HbA1C more than 8 was higher [8.2] when compared to the group with HbA1C of less than 6.5 was lower[8.06] with high significance.[128]

In the study done by Jabeen F et al.51 diabetic subjects and 55 controls were studied with an average age of 52 years. 55% of the studied population with diabetes were males. The study revealed a higher mean platelet volume in subjects with poor glycemic control compared to the well-controlled population grouped according to the HbA1C values. In the study the male diabetics had an average MPV of 8.9fL.whereas to female diabetics had an MPV value of 9.53Fl with a similar HbA1C values [6.7]. In the current study also a similar picture of larger MPV was noted in the female diabetic population but it was not statistically significant[129].

In an Indian study done by Kodiette et al. 255 diabetic patients was studied with match controls. 65% of the studied population were males with an average age of 55years. The average duration of diabetes was 6.5 years, BMI 25,FBS150,PPBS252.

The study demonstrated as statistically significant increase in MPV with rising HbA1C. The main HbA1C in the studied population was 9.13Fl. In the group with HbA1C of less than 6.5 showed an average MPV of 7.95 whereas in the group with HbA1C value of 6.5 and more showed an average MPV of 8.35 [130].

Papanas N et al. in 2004 studied 416 subjects with 265 diabetic patients with an average age of 67 years. The studied population consisted 51% of females and an average of 14 years history of diabetes. In the study the diabetic population had 14Fl of MPV compared to 7Fl in the non-diabetic population evaluated in the study[131].

Zuberi et al studied a total of 600 subjects with 200 diabetic patients with the mean age of 40 and found that the mean platelet volume increased with increasing glycemic status.

In a study done in Mangalore which was similar to the current study with 100diabetic patients with 50 controls. The study focused on the use of insulin and oral hypoglycemic agents on the mean platelet volume in diabetic subjects. The MPV values in the study were similar to the current study with the diabetic population on OHAs was around 8.08 fL and controls with 7.96 Fl of MPV values. The majority of population in the current study was on OHAs alone for the treatment of diabetes and had a similar MPV values.

The majority of population in the current study was on oral hypoglycemic agents alone for the treatment of diabetes and had a similar Mean Platelet Volume values.

STUDY	SHAH B et al.	JABEEN F et al.	KODIETTE et al.	PAPANAS N et al.	SHIMODARA M et al.	ZUBERI M et al.	VERNEKAR P et al.	CURRENT STUDY
SUBJECTS	13,021	106	506	416	1876	612	150	100
MEN WOMEN	48%: 52%	51%: 49%	61%: 39%	49%: 51%	60%: 40%	55%: 45%	50%: 50%	42%: 58%
Age,y mean+SD	47 +/-9.0	52 +/- 7	55 +/- 7	67.4 +/- 9.5	57.4 +/- 10.32	40 +/-10.2	59.5 +/- 9.24	52.12 +/- 9.33
MPV (HbA1C)	8.09 (<6.5) 8.24(6.6-7.9) 8.35(>8%)	8.38 +/- .25(<5.6) 9.53+/- .23(>6.5)	7.95+/- 2.53(<6.5) 8.35+/- .724(>6.5)	7.1+/- 1.2(ND) 14.2+/- 2.2(D)	9.97+/- .69(ND) 10.12+/- .79(IGT)	8.63(ND) 8.98(DC) 9.34(D-NC)	7.96(ND) 7.53(I) 8.08(O)	7.29+/-.786 (<7) 7.9+/-.659(7.1-8) 8.76+/- 1.068 (>8)

LIMITATIONS OF STUDY

There are a few limitations to the study that is needed to be mentioned

1) There were only 100 patients in the study. Sample size was small.
2) The study was confined to a small geographical area.

CONCLUSION

The conclusions of this study are following:

1) This study has shown an elevation in Mean Platelet Volume in patients with increased HbA1C (glycated hemoglobin) values, thus indicating poor control of diabetes and, it can be stated that an increase in Mean Platelet Volume is directly proportional to the numerical value of HbA1C (glycated hemoglobin) and inversely related to the control of diabetes. Statistically significant association was found with glycated hemoglobin (HbA1C) (P-value =.0001) and mean platelet volume.

2) Statistically significant association was found with duration of diabetes(p=.0001) and mean platelet volume.

3) The study did not find a statistically significant relation between Body Mass Index, lipid profile(total cholesterol, High density lipoproteins, Triglycerides, Low density lipoproteins) and Mean Platelet Volume.

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PROFORMA

1.Name2. Age/Sex

3. Marital Status

4. Educational Qualification 5.Occupation

6. Address 7.Contacct no

8.Height(cm) 9.Weight(kg) 10.BMI

11. Duration of diabetes 12. Treatment duration

13. Past medical history

14.SHT15. History of thyroid diseases/CAD

16.Smoking history 17. Alcohol history

LABORATORY FINDINGS

1.CBCHb TC DC Plt MPV PDW

2. FBS,PPBS3.HbA1C

4.FLPT.Chol HDL LDL

5.BLD UREA 6.S. CREATININE

7. TFT T3 T4 TSH

தகவல் படிவம்

மதிப்பிற்குரிய அய்யா / அம்மையீர்,

நீரிழிவு நோயாளிகளின் இரத்த சர்க்கரை அளவு கட்டுப்பாட்டின் கீழ் இருப்பது அவசியம். காட்டுப்பாட்டின் கீழ் இல்லையெனில், இரத்தத்தில் உள்ள பிளேட்டிலட் அணுக்களில் மாற்றம் உண்டாகும். பிளேட்டிலட் மாற்றம் அடையவதால், இரத்த குழாய்களில் அடைப்பு ஏற்பட வாய்ப்பு உள்ளது. இந்த மாற்றத்தை சீக்கிரமாக ஒரு சிறிய இரத்த பரிசோதனையின் மூலம் கண்டறியலாம். விரைவில் கண்டறிவதன் மூலம் இரத்த சர்க்கரை அளவைக் குறைப்பதோடு, பிளேட்டிலட்டில் ஏற்படும் மாற்றத்தையும், இரத்த குழாயில் ஏற்படும் அடைப்பையும் தடுக்கலாம்.

அதற்கு உங்கள் முழு சம்மதம் வேண்டியே இந்த படிவம் வழங்கப்படுகிறது. தாங்கள் இந்த ஆய்வில் பங்கேற்ற சம்மதிக்கும் பட்சத்தில் இந்த படிவத்தை முழுவதும் படித்து பார்த்து முழு மனதுடன் ஒப்புதல் அளிக்க கையொப்பமிடுமாறு கேட்டுக் கொள்கிறேன்.

மேலும் இந்த ஆய்வினால் உங்கள் உடலுக்கோ மனதிற்கோ இன்னல் ஏற்படாது என்றும் தேவையற்ற பரிசோதனைகள் எதுவும் செய்யப்படாது எனவும் உறுதி கூறுகிறேன்.

நாள் :

நோயாளி / உறவினரின்
கையொப்பம்
இடது பெருவிரல் ரேகை
(மருத்துவரால் படித்துக்காட்டப்பட்டது)

சுய ஒப்புதல் படிவம்

நீரிழிவு நோயாளிகளின் இரத்த சர்க்கரை அளவைப் பொருத்து பிளேட்டிலட் தொகுதி அர்த்தத்தில் ஏற்படும் மாற்றம் தொடர்பான ஆய்வு

ஆராய்ச்சி நிலையம் : அரசு ஸ்டான்லி மருத்துவமனை
சென்னை - 600 001.

பங்கு பெறும் நோயாளியின் பெயர்: வயது :

பங்கு பெறும் நோயாளியின் எண் : பாலினம் : ஆண் ☐ பெண் ☐

நோயாளியின் விலாசம் :

நோயாளி இதனை (✓) குறிக்கவும்.

மேலே குறிப்பிடப்பட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டது. என்னுடைய சந்தேகங்களை கேட்கவும். அதற்கான தகுந்த விளக்கங்களை பெறவும் வாய்ப்பளிக்கப்பட்டது. ☐

நான் என்னை இவ்வாய்வில் தன்னிச்சையாகதான் பங்கேற்க அனுமதிக்கிறேன். எந்த காரணத்தினாலோ எந்த கட்டத்திலும் எந்த சட்ட சிக்கலுக்கும் உட்படாமல் என்னை இவ்வாய்வில் இருந்து விலக்கி கொள்ளலாம் என்றும் அறிந்து கொண்டேன். ☐

இந்த ஆய்வு சம்பந்தமாகவோ, இதை சார்ந்த மேலும் ஆய்வு மேற்கொள்ளும் போதும் இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளை பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன். என்னை ஆய்வில் இருந்து விலகிக் கொண்டாலும் இது பொருந்தும் என அறிகிறேன். ☐

இந்த ஆய்வின் மூலம் கிடைக்கும் தகவல்களையும், பரிசோதனை முடிவுகளையும் மற்றும் சிகிச்சை தொடர்பான தகவல்களையும் மருத்துவர் மேற்கொள்ளும் ஆய்வில் பயன்படுத்திக் கொள்ளவும் அதை பிரசுரிக்கவும் என் முழு மனதுடன் சம்மதிக்கிறேன். ☐

இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக் கொள்கிறேன். எனக்கு கொடுக்கப்பட்ட அறிவுரைகளின்படி நடந்த கொள்வதுடன் இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்று உறுதியளிக்கிறேன். என் உடல் பாதிக்கப்பட்டாலோ அல்லது எதிர்பாராத வழக்கத்திற்கு மாறான நோய்க்குறி தென்பட்டாலோ உடனே அதை மருத்துவ அணிக்கு தெரிவிப்பேன் என உறுதி அளிக்கிறேன். ☐

பங்கேற்பவரின் கையொப்பம் ..... இடம் ..... தேதி

கட்டைவிரல் ரேகை (இந்த படிவம் படித்து காட்டப்பட்டு புரிந்து கைரேகை அளிக்கின்றேன்)

பங்கேற்பவரின் பெயர் மற்றும் விலாசம் .....

ஆய்வாளரின் கையொப்பம் ..... இடம் ..... தேதி

ஆய்வாளரின் பெயர் .....

INSTITUTIONAL ETHICAL COMMITTEE, STANLEY MEDICAL COLLEGE, CHENNAI-1

Title of the Work : Study on the effect of Glycemic control on mean Platelet volume in type 2 diabetic patients on treatment.

Principal Investigator : Dr. Doron Susan Mathew

Designation : PG in MD (General Medicine)

Department : Department of General Medicine
Government Stanley Medical College,
Chennai-01

The request for an approval from the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 02.07.2014 at the Council Hall, Stanley Medical College, Chennai-1 at 2PM

The members of the Committee, the secretary and the Chairman are pleased to approve the proposed work mentioned above, submitted by the principal investigator.

The Principal investigator and their team are directed to adhere to the guidelines given below:

1. You should inform the IEC in case of changes in study procedure, site investigator investigation or guide or any other changes.
2. You should not deviate from the area of the work for which you applied for ethical clearance.
3. You should inform the IEC immediately, in case of any adverse events or serious adverse reaction.
4. You should abide to the rules and regulation of the institution(s).
5. You should complete the work within the specified period and if any extension of time is required, you should apply for permission again and do the work.
6. You should submit the summary of the work to the ethical committee on completion of the work.

K Vasanthan

MEMBER SECRETARY,
IEC, SMC, CHENNAI

MASTER CHART

SN	A	G	H	W	BMI	DD	RX	TESTAB	HB	TC	PLT	MCV	WBC	RBC	HCT	MCH	MCHC	RDW	ESR	LY	MO
1	44	F	1.65	70	25.7	5	O+	N N N 100/70	11	12900	5.5	7.6	15	126	176	7.4	356	188	235	38	32	0.8	80	8.1	5.1
2	65	F	1.58	65	26	5	O	N N N 100/70	12	8100	3.9	7.4	14	120	150	7.1	196	178	120	40	36	1	68	8.9	4.5
3	44	M	1.63	70	26.3	3	O	Y Y Y 120/70	14	8600	3.2	7.4	15	230	300	8.9	220	190	130	37	38	1.2	77	8.8	0.5
4	70	F	1.54	60	25.3	5	O	Y N N 170/80	11	7600	5.9	7.5	14	130	170	7.3	230	170	140	34	40	0.9	110	10	2
5	56	M	1.74	80	26.4	5	O	N N N 140/80	11	4600	1.8	7.7	14	210	275	8.1	240	140	136	32	32	0.7	117	11	3.2
6	65	M	1.68	72	25.5	1	O+	N N Y 110/70	11	7700	3.6	7.6	13	256	301	8.6	256	180	198	30	42	1.1	150	10.5	4.4
7	50	F	1.6	58	22.7	3	O	Y N N 100/70	11	7200	3.2	7.1	13	110	140	5.9	216	160	110	46	34	0.7	74	7.4	3.8
8	60	F	1.56	56	23	10	O	Y N N 140/80	11	7200	2.5	9.2	13	400	386	9.7	230	130	127	44	37	0.5	83	4.3	4
9	41	F	1.58	76	30.4	1	O	N N N 110/70	10	9400	3.4	8.5	13	156	256	10	286	140	134	31	12	0.2	98	4.9	3
10	57	F	1.63	60	22.6	2	O	N N N 120/80	11	7400	2.4	8.2	13	306	416	11	210	134	114	42	16	0.7	110	11.2	2.7
11	48	F	1.45	65	30.9	2	O	N N N 120/72	11	9000	1.9	7.1	12	132	197	5.8	180	110	110	48	19	0.9	129	10.3	5
12	70	F	1.59	70	27.7	7	O	N N N 116/78	12	8400	3.4	9	16	116	200	8	172	130	98	32	19	0.7	74	8.7	0.8
13	61	M	1.6	60	23.4	15	O	N N N 140/80	11	8100	3.4	8.5	16	130	180	7.6	160	124	100	48	19	1	197	9.4	0.5
14	50	F	1.6	55	21.5	8	O	Y N N 140/90	11	5600	3.8	7.8	15	326	420	11	250	128	200	38	19	1	147	9	0.9
15	47	F	1.65	65	23.9	2	O	N N N 110/80	11	9700	4.6	7.7	15	130	174	5.6	176	134	112	44	20	0.3	150	5	3
16	64	M	1.65	80	29.4	1	O	Y Y Y 150/90	12	8400	2.8	7.1	13	105	158	6	148	88	98	40	21	0.3	99	4.8	2
17	38	M	1.68	75	26.6	4	O	N Y Y 110/70	12	6700	5.1	7.5	14	169	222	7	182	78	110	48	29	0.4	88	5.4	1
18	55	M	1.65	68	25	4	O	Y Y Y 110/70	11	9300	4.7	7.9	13	140	188	7.9	222	100	134	39	23	0.3	74	6.2	0.5
19	53	M	1.71	76	26	1	O	N Y Y 110/70	11	9000	1.8	5.2	9	170	246	6.4	128	102	156	48	21	0.1	174	10.1	3
20	42	F	1.6	70	27.3	4	O+	N N N 120/86	13	4200	3.1	7.1	14	300	210	11	168	73	114	42	30	0.2	125	9.4	4
21	35	F	1.61	72	27.8	5	O	N N N 130/74	12	3800	4.4	7.3	14	148	157	6.9	170	89	101	48	31	0.1	124	9.3	5
22	49	M	1.68	73	25.7	1	O	Y Y N 150/80	14	8400	3.5	7.5	11	199	211	9.1	114	95	103	40	12	0.6	131	8.7	2.5
23	56	F	1.59	60	23.9	1	O	N N N 140/70	13	8900	3.2	7.8	11	159	190	8.4	186	107	126	48	12	0.4	142	8.8	3.2
24	37	M	1.6	70	27.3	2	O	Y Y Y 140/80	13	5900	2.5	8	14	160	200	8.1	192	113	131	32	15	1	178	8.9	5.6
25	40	M	1.57	65	26.4	1	O	Y N Y 120/80	13	6600	3.8	6.9	13	102	158	5.6	200	140	122	40	13	0.2	144	10.7	5.2
26	50	F	1.58	63	25.1	1	O	N N N 110/60	12	8050	2.5	10	15	164	246	11	180	132	135	30	31	0.3	156	11.1	5
27	61	F	1.53	43	18.2	8	O	N N N 120/60	11	7540	2.7	9.2	13	128	178	7.2	206	182	134	44	20	0.2	88	8.8	3
28	49	F	1.43	54	26.2	4	O+	N N N 120/80	12	5460	4	7.7	11	295	264	10	165	111	134	38	14	0.2	97	8.6	4.2
29	43	F	1.46	42	19.8	12	O	N N N 110/70	9	7910	5.1	8.5	12	182	222	7.5	260	154	144	37	13	0.3	130	11.1	4.8
30	61	F	1.64	84	31.2	10	O	N N N 120/70	13	8950	3	8.6	12	244	260	9	168	123	132	44	19	0.7	154	9.9	4.9
31	67	M	1.67	61	21.9	22	O	Y Y Y 130/90	13	9700	2.9	8.6	12	156	200	7.6	170	141	120	38	30	0.3	174	9.6	3
32	67	F	1.48	59	27.1	12	O	N N N 90/60	12	7101	2.4	8.1	12	112	138	7.2	178	132	130	36	19	0.2	181	8.7	2
33	45	F	1.59	73	29	4	O	N N N 100/70	12	8320	2.9	9.7	14	217	232	9.4	198	151	146	22	28	0.4	167	10.1	3
34	63	F	1.43	66	32.2	12	O	N N N 120/60	12	7370	2.9	9.3	13	138	212	6.7	286	180	144	39	19	0.5	88	5.1	2
35	50	F	1.42	60	29.8	1	O	N N N 130/80	13	8420	2.6	7.9	11	169	174	8.8	168	142	142	28	30	0.1	87	5.8	2.5
36	40	F	1.5	71	31.6	2	O	N N N 130/80	12	9350	4.8	8.2	12	147	190	7.4	252	178	180	20	13	0.8	94	6.9	2.6
37	55	M	1.56	48	19.7	6	O	N Y Y 110/70	14	7900	2.4	8.3	12	132	159	6.2	315	198	210	32	19	0.5	96	6.8	3
38	55	F	1.46	55	25.8	2	O	N N N 110/70	13	5460	2.1	10.8	16	220	270	11	244	189	130	40	31	0.4	144	7.6	2.5
39	57	F	1.45	67	31.9	6	O+	N N N 110/70	13	9030	2.4	8.6	12	220	282	9.2	174	112	124	43	19	0.9	198	7.4	2.4
40	51	M	1.55	60	25	1	D	N Y Y 110/70	13	9270	3	7.8	11	137	202	6.1	178	132	135	38	26	0.1	144	10.9	3.6
41	47	F	1.67	67	24	1	O+	N N N 120/80	10	7420	3	8.9	15	412	562	14	352	182	256	40	23	0.2	188	10.7	3.4
42	66	F	1.56	66	27.1	7	O+	Y N N 150/70	11	5400	3.2	9.7	14	171	197	9.6	250	152	208	40	21	0.6	98	6.4	2.4
43	40	M	1.6	50	19.5	5	O	Y N N 140/80	10	5240	4	8.7	12	199	210	9.1	196	111	130	40	29	0.2	190	6.9	2
44	40	M	1.7	60	20.8	3	O	Y Y Y 140/90	11	5500	3	7.2	10	159	174	8.4	230	110	164	42	31	0.8	170	8.1	2
45	38	F	1.54	57	24	2	O	N N N 120/80	12	6500	4	7.1	11	143	154	7.7	185	98	121	44	31	1	140	8.9	5
46	47	F	1.63	60	22.6	7	O	N N N 130/70	10	7500	2.4	9.7	13	164	174	10	193	108	140	44	21	0.2	150	11.1	4.3
47	48	M	1.7	61	21.1	3	O	N N N 120/80	10	5700	2.5	7.1	12	128	154	7	174	112	110	32	28	0.2	175	8.9	0.9
48	56	F	1.48	58	26.5	6	O	N N N 110/70	12	5400	2.7	9.6	13	285	364	11	256	114	210	29	13	0.5	150	7.6	1.4
49	58	M	1.52	61	26.4	2	O	N N N 110/80	10	4500	3.4	6.9	11	134	184	6.9	171	78	110	31	31	0.9	124	8.8	1.3
50	48	M	1.67	65	23.3	4	O	N Y N 130/70	11	5780	3.5	9.4	13	295	356	13	220	106	164	44	17	0.2	132	9.4	1.3
51	40	M	1.72	62	21	2	O	N N N 142/80	11	5470	3.2	7.6	10	182	223	8.8	180	100	144	32	14	0.1	188	10.1	2.4
52	60	F	1.52	70	30.3	10	O	N N N 130/70	11	6780	2.4	10	11	244	322	10	190	120	132	40	31	0.2	199	5	2.8
53	63	F	1.63	72	27.1	3	O	N N N 146/80	12	7500	1.5	7.7	11	156	213	8	200	162	188	39	22	0.4	100	5.5	2.4
54	60	M	1.5	49	21.8	2	O	Y Y Y 150/90	11	6700	1.7	7.3	11	112	342	8.7	222	172	122	37	25	0.5	110	5.6	3.5
55	60	M	1.61	50	19.3	5	O	N Y Y 140/70	11	4700	1.9	8.9	12	217	422	11	200	160	110	41	27	0.9	161	4.5	3.7
56	63	F	1.51	51	22.4	3	O	N N N 140/80	11	8700	3.5	7.4	11	167	178	7.3	147	107	98	44	28	0.1	80	4.9	4
57	50	M	1.58	56	22.4	7	O	N Y Y 110/80	11	9700	3.7	10.5	14	138	178	10	152	98	96	45	31	0.2	180	9.4	2.3
58	60	F	1.48	54	24.7	2	O	N N N 100/70	11	5600	2.4	6.9	10	169	176	7.9	160	96	94	48	21	0.3	130	8.5	1
59	65	F	1.5	50	22.2	5	O	N N N 100/80	11	7600	2.7	9.9	13	147	178	11	170	86	111	38	13	0.2	112	4.9	2.3
60	50	M	1.67	70	25.1	1	O	N Y Y 110/80	10	4700	2.8	6.9	10	232	178	8.5	180	94	140	31	18	0.6	142	5.7	1.8
61	52	F	1.65	77	28.3	2	O	Y N N 120/80	11	9800	2.9	7.1	12	171	141	6.3	260	140	196	29	23	0.7	162	7.9	0.7
62	60	M	1.56	72	29.6	1	O	N Y Y 130/84	12	5800	1.5	7.3	10	132	121	6.5	220	144	170	35	31	0.2	142	8.3	0.9
63	65	F	1.61	68	26.2	6	O	N N N 140/80	11	8700	2.6	8.9	13	180	199	11	200	122	150	36	16	0.4	142	6.7	3
64	62	M	1.54	59	24.9	12	O	N N N 140/90	10	8500	3.7	10.1	14	220	349	11	180	102	120	44	18	0.2	142	8.7	0.3
65	60	F	1.63	70	26.3	9	O	N N N 140/80	10	4800	3.9	10.5	13	175	413	15	160	107	111	40	21	0.6	183	7.6	0.7
66	40	M	1.62	62	23.6	4	O	N Y Y 130/76	11	5700	3.7	7.7	11	196	212	7.3	151	108	121	30	29	0.3	192	5.9	5.3

67	45	F	1.69	64	22.4	3	O	Y	N	N	100/70	10	6700	3.9	7.4	11	150	170	6.1	162	104	131	39	21	0.5	199	9.5	0.7
68	55	M	1.67	72	25.8	5	O	N	Y	Y	110/80	12	9800	1.9	8.7	13	126	156	7.8	189	88	171	32	31	0.2	121	4.7	0.9
69	45	M	1.58	74	29.6	3	O	N	Y	Y	100/70	11	5700	1.9	7.4	11	156	174	7.6	249	160	192	22	25	0.4	99	9.7	5
70	61	F	1.6	61	23.8	8	O+	N	N	N	110/80	11	6700	1.7	9.9	12	176	183	11	190	130	152	32	13	0.6	148	9.6	4.5
71	37	F	1.5	53	23.6	2	O	N	N	N	100/70	11	4500	2.6	7.1	11	166	210	6.9	160	104	101	48	18	0.9	160	4.7	3.5
72	39	M	1.6	54	21.1	1	O	N	Y	Y	110/80	12	5700	2.5	7	11	174	230	7.1	200	108	130	36	15	0.3	110	4.8	5
73	45	M	1.7	60	20.8	3	O	N	Y	Y	100/60	12	5700	1.5	7.7	12	200	220	8.1	190	110	121	42	23	0.3	88	4.9	3
74	48	F	1.52	57	24.7	1	O	N	N	N	120/78	10	8700	1.6	6.9	11	201	312	7.8	160	121	107	42	31	0.2	79	9.7	2
75	51	F	1.6	56	21.9	1	O	Y	N	N	160/90	10	8900	2.6	7.4	11	146	204	7.9	170	100	127	37	30	1	128	9.8	4
76	36	M	1.56	45	18.5	1	O	N	Y	Y	140/80	10	8600	4	8.7	12	222	343	10	160	88	111	40	24	0.1	174	8.7	3
77	45	F	1.53	60	25.6	4	O	N	N	N	130/76	11	8700	2.8	8	12	232	354	9.3	172	77	108	41	19	1.1	96	9.7	2
78	51	M	1.59	56	22.2	6	O	N	Y	Y	110/74	11	6700	4.3	9.1	14	210	300	8.4	192	94	112	32	13	1.1	102	6.5	2.4
79	67	F	1.62	60	22.9	8	O	Y	N	N	112/82	12	7600	4.2	10	13	240	342	11	182	92	132	34	31	1	78	5	5
80	61	F	1.64	63	23.4	5	O	N	N	N	110/70	11	8500	4	9.8	14	210	344	9.8	181	104	152	31	21	0.3	190	4.6	3
81	52	M	1.65	65	23.9	3	O	N	N	N	100/60	12	9600	3.4	8	13	310	412	8.8	211	103	179	30	14	0.2	184	7.4	3.4
82	45	F	1.66	53	19.2	2	O	Y	N	N	100/80	11	8700	3.5	7.4	13	400	200	7.6	230	104	169	27	19	0.3	88	6.8	3.1
83	64	M	1.71	65	22.2	7	O	Y	Y	Y	162/90	10	8600	2.5	8.9	13	140	213	9.4	250	108	191	27	23	0.7	89	6	2.3
84	36	M	1.58	54	21.6	1	O	N	N	N	100/70	11	5600	2.4	7.6	13	122	214	8.3	264	180	211	26	24	0.8	100	5	0.5
85	47	F	1.57	64	26	2	O	N	N	N	110/70	10	7900	3.5	7	13	142	212	6.9	231	108	200	22	31	0.5	172	9	0.8
86	46	F	1.58	47	18.8	1	O	N	N	N	128/80	10	8700	3.7	7.1	12	162	182	7.2	275	188	230	30	24	0.3	163	8	4.4
87	43	M	1.66	57	20.7	4	O	N	N	N	130/80	9	6800	3.7	8.5	13	132	174	8.4	250	129	200	31	21	0.9	121	7	0.5
88	53	F	1.51	64	28.1	2	O	N	N	N	140/80	10	9800	2.4	8.2	14	121	178	7.4	242	168	199	33	26	0.2	190	7.5	0.4
89	57	F	1.53	65	27.8	5	O	N	N	N	130/80	11	8500	2.5	8.8	14	140	162	7.3	214	104	177	31	13	0.2	162	5.6	2.3
90	63	M	1.74	66	21.8	6	O	Y	Y	Y	130/80	10	8700	3.5	9.2	14	170	181	9.4	215	103	111	41	31	0.2	69	7.6	2.7
91	45	M	1.64	65	24.2	4	O+	Y	N	N	120/90	12	9500	1.5	9	13	190	219	8.9	260	102	190	29	21	0.4	62	9	3.9
92	42	F	1.58	51	20.4	2	O	N	N	N	130/80	11	5600	1.6	8.1	13	120	214	7.9	251	128	181	37	22	0.2	111	8.7	0.9
93	67	F	1.54	57	24	8	O	Y	N	N	140/80	12	4500	1.7	10.5	14	210	220	11	223	103	174	33	29	0.5	134	6	0.4
94	63	M	1.59	59	23.3	7	O	N	Y	Y	170/80	11	5600	2.5	9.8	14	300	310	9.3	194	66	128	35	25	0.9	192	8	2.6
95	45	F	1.48	58	26.5	9	O	N	N	N	140/80	12	7600	2.6	10.1	14	342	304	12	161	78	114	34	21	0.5	172	6	4.7
96	43	M	1.57	60	24.3	3	O	Y	N	N	110/80	12	6700	1.7	7.9	13	210	300	7.4	154	88	128	40	13	0.3	132	7.6	2.1
97	41	F	1.61	66	25.5	2	O	N	N	N	130/80	11	7600	1.7	7.3	13	146	172	8.3	192	94	130	41	16	0.2	96	4.7	0.9
98	52	F	1.51	65	28.5	5	O	N	N	N	170/80	11	8700	1.8	8.4	13	136	178	8.6	171	88	126	39	17	0.6	82	8	0.7
99	56	F	1.58	63	25.2	6	O	Y	N	N	160/80	11	6700	1.6	8.7	13	147	183	7.9	223	170	174	28	19	0.2	78	9	2.5
100	57	M	1.62	61	23.2	3	O	Y	Y	Y	130/80	10	7600	3.5	8.1	13	152	164	7.1	161	86	105	40	21	0.4	110	7	3.7

KEYS TO MASTER CHART

- SN SERIAL NO
- A AGE
- G GENDER
- H HEIGHT
- W WEIGHT
- BMI BODY MASS INDEX
- DD DURATION OF DIABETES
- RX TREATMENT
- O ORAL HYPOGLYCEMICS ALONE
- O+I ORAL HYPOGLYCEMIC AND INSULIN
- H HISTORY OF HYPERTENSION
- S HISTORY OF SMOKING
- A HISTORY OF ALCOHOL
- BP BLOOD PRESSURE
- Hb HEMOGLOBIN
- TC TOTAL COUNT
- PLT PLATELET COUNT
- MV MEAN PLATELET VOLUME
- PW PLATELET DISTRIBUTION WIDTH
- FB FASTING BLOOD SUGAR
- PP POST PRANDIAL BLOOD SUGAR
- H1C GLYCATED HEMOGLOBIN
- CH CHOLESTEROL
- TG TRIGLYCERIDES
- LD LOW DENSITY LIPOPROTIEN
- HD HIGH DENSITY LIPOPROTIEN
- UR UREA
- CR CREATININE
- T3 T3-Triiodothyronine
- T4 T4-Thyroxine
- TH Thyroid Stimulating Hormone

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STUDY ON THE EFFECT OF GLYCEMIC CONTROL ON MEAN PLATELET

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A Dissertation on

STUDY ON THE EFFECT OF GLYCEMIC CONTROL ON MEAN PLATELET VOLUME IN TYPE 2 DIABETIC PATIENTS ON TREATMENT

Submitted to

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CHENNAI – 600032

In partial fulfilment of the Regulations
for the Award of the Degree of

M.D. BRANCH - I

GENERAL MEDICINE

DEPARTMENT OF GENERAL MEDICINE

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